Exhibit 1 S 1400

To the City Court of Helsinki

in the Case - Pentti Kalevi Aho / Suomen Tupakka Oy and Oy Rettig Ab concerning Claim of Damages

Suomen Tupakka's Brief No. 10

12/7/90

THE TOBACCO AND HEALTH CONTROVERSY

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1. INTRODUCTION

1.1 Foreword To The Subject

The Complaints are based on the claims that plaintiff Pentti Aho is suffering from chronic bronchitis, emphysema and cancer of the larynx as a result of his smoking. The main themes of the plaintiff side's determination of cause have so far been two:

Firstly, it has been emphatically claimed on the part of plaintiff that medical science has definitely proved that smoking is the by far most important cause of those diseases from which plaintiff suffers (general causation); and secondly, that there are no doubts as to this general causation, but there exists, in practice, a unanimous understanding in the medical profession of its definitive proof.

No evidence has actually been presented by the plaintiff side as to the individual causes of Pentti Aho's own diseases, but in his case the individual causation has been derived from the general causal hypothesis on the basis of the belief that the diseases concerned virtually exclusively are caused by smoking and that they also (according to the unanimous understanding of medical science) sooner or later are necessary consequences of smoking.

The above described reasons of the Complaint as to cause or causes of plaintiff's diseases follow the so-called official stance in Finland which has mainly been formulated by the Medical Board and certain health organizations,

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and which has been consistently applied in the health education activities pertaining to tobacco, and the extent to which they are embraced, which is periodically measured by the Medical Board in the polls repeatedly referred to in this case. The corollary of this is the allegation, which also has been stated as an additional reason of the Complaint, that the tobacco industry always and consistently would have, against better knowledge, denied that any detriment or even any risk could result from smoking, and that this stance, being contradictory to the unanimous understanding of medical science, would keep the public in uncertainty as to the health detriments so proved to be caused by smoking.

The basic claims of the plaintiff side are as such so impossible that they would not require any reply in detail. However, since the causal hypothesis of smoking and many diseases is widely supported even among professionals, not in the form described by the plaintiff side, but anyway, an explanation in detail of the issue is appropriate.

As far as known to Suomen Tupakka, the tobacco industry has at the same time as medical science accepted and acknowledged that smoking is a risk factor associated with human health. The question what the nature and magnitude of the risk has naturally varied with the assessments of medical science at any given time. Medical science defines risk factors as factors which have been identified as, so to speak, "on the scene", but which generally, and especially in individual cases, may or may not be causally related to the development of disease.

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The above described contrast is consequently not so sharp as one could be led to believe from the anti-smokers' declarations and the columns of the press. The reason for the problem is that those involved have largely so far not wanted to settle for a description of smoking as a risk factor, but have gone further and adopted the risk hypothesis as causal. The reason for this may be a natural need and desire to respond to a significant scourge to human health. It may also stem from a belief that people are not prepared to give up a risky habit unless they are made to believe that an unavoidable evil will follow therefrom. Since the tobacco industry on its own part cannot accept these views, the differences of opinion have by the lapse of time and in certain places developed into a religious war, which has disengaged itself from facts, and from which the tobacco industry has tried to stay apart.

Although there has been, for as long as can be remembered, a commonly held belief among the public at large that tobacco is injurious to health in a variety of ways, in the scientific community there has been and continues to be a substantial controversy as to whether a causal relationship has been scientifically established between cigarette smoking and human disease. Moreover, the public health agencies and similar authorities who have come to the opinion that the case against smoking is sufficient for them to act did not during modern history do so until the relatively recent past.

The purpose of this document is to address the history, and in part the content, of the scientific controversy surrounding smoking. It is submitted to demonstrate the falseness of the claim of the plaintiff side that the tobacco companies have acted in disregard of unanimously accepted

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scientific proof and that they are therefore both civilly and criminally liable. The intention is not that the City Court would undertake to decide the smoking and health controversy; indeed, that controversy cannot be resolved until science develops the requisite knowledge to answer the many questions that presently exist. However, since the causal hypothesis is driven in Finland so detached from facts and with so exacerbated expressions as appears from Professor Aurejarvi's last brief (Aurejarvi, 9/13/90, for example pages 3-9), and when even scientists in our country are not permitted to doubt the official stance, or to talk about expressing doubts, a review of the history of the controversy, which to a large extent has been kept hidden from the Finnish population, may be useful.

1.2 Development of Determination of Cause

Before World War II, medical science was preoccupied with discovering the causes and cures of infectious diseases. Its concepts of cause grew from that experience and were ultimately embodied in a series of criteria -- Koch's Postulates -- by which proof of causation was established. Focus was fixed upon individual causal agents, such as the tubercular bacillus, and experiments in which such agents produced disease in the laboratory provided the standard methodology of proof.

With the war-assisted development of penicillin and antibiotics, the fight against infectious diseases was largely won, with life spans increasing

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as a result of these advances, along with general improvements in diet and living conditions. But medical science was increasingly challenged by chronic diseases, such as cancer and heart disease, that appeared to develop over very long periods, often encompassing most of the individual's life span. It was gradually recognized that these diseases were extremely complex and that the single factor causal concepts demonstrable for infectious diseases would not apply. Disciplines, such as epidemiology, were adapted and expanded, and new concepts of causation, including hypotheses relating to multifactorial causation and constitutional factors, were suggested.

A major area of these developments in the 1950s and 1960s arose in the investigations of possible relationships between smoking and health, culminating in the Report to the United States Surgeon General in 1964 (hereinafter, "the 1964 Terry Report"). The 1964 Terry Report recognized that causation was not scientifically demonstrable by previously accepted standards of proof, and proposed to substitute a subjective judgment based upon specifically enumerated criteria. The 1964 Terry Report stated as follows:

Statistical methods cannot establish proof of

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a causal relationship in an association. The causal significance of an association is a matter of judgment which goes beyond any statement of statistical probability. To judge or evaluate the causal significance of the association between the attribute or agent and the disease, or effect upon health, a number of criteria must be utilized, no one of which is an all-sufficient basis for judgment. these criteria include:

a) The consistency of the association
b) The strength of the association
c) The specificity of the association
d) The temporal relationship of the association
e) The coherence of the association

Thus, the Report carefully distinguished the scientific demonstration of cause from the formation of a judgment that a body of information warrants public health action.

Had the 1964 Terry Report, consistent with its criteria, asserted only that the Committee judgment was that public health action was warranted, the debate might well have been limited to whether public health action was prudent in light of the existing information, even if it were recognized as being insufficient to establish causation scientifically. Had this been the case, the last three decades might well have seen not only a very different kind of debate, but also less resort to litigation -- at best an ineffective means to resolve this sort

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of controversy. But the 1964 Terry Report went on to confuse the distinction it had so carefully drawn. It asserted that smoking was a cause of lung and larynx cancer in men and of chronic bronchitis, rather than pointing out, more honestly, that smoking was a risk factor for these diseases and that this association was sufficient for public health action.

The 1964 Terry Report thus fueled the flames of the controversy on two levels: first, has smoking been scientifically established as a cause of human disease; and, second, is public health action warranted. And, as is so often the case, the debate raged without regard to which of the two issues was being addressed by any given argument. Thus, claims of proof of causation -- based upon epidemiologic studies that had considerable possible public health significance -- were hotly disputed on the ground that statistics could not scientifically prove cause and effect.

1.3 "Those Who Were Wrong." A Perspective 1989/90

A recent paper and subsequent discussion has served both to give perspective to this debate and, at long last, to admit what should have been agreed all along: that science has not yet developed the methods and tools by which to prove scientifically that smoking is or is not a cause of human disease.

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In "Those Who Were Wrong," in the American Journal of Epidemiology, Prof. J.P. Vandenbroucke discussed the analyses and arguments made by three of the eminent scientists who disagreed with the smoking-causation claim in the 1950s and 1960s. (Vandenbroucke 1989) Those were Sir Ronald Fisher, the "father" of modern statistics and a preeminent geneticist, Dr. Joseph Berkson, a leading biometrician at the renowned Mayo Clinic in the United States, and Professor Hans Eysenck, a renowned psychologist at and Head of the Institute of Psychology, University of London. Characterizing their work as "well-written and cogent papers that might have become textbook classics for their impeccable logic and clear exposition of data and argument," Vandenbroucke writes that he would likely have agreed with them at the time. (Professor Eysenck's work was described by Vandenbroucke as "an argument of breathtaking elegance . . . .")

Dr. Sander Greenland's discussion of this paper (Greenland 1990), despite his strong views against smoking, and Vandenbroucke's response are sufficiently short and illuminating to warrant reproduction in full. Dr. Greenland recognizes that a causal relationship can never be proved by epidemiological evidence, disagreeing only with whether the epidemiological evidence was sufficient to warrant prudent public health action, not even whether it was sufficient to scientifically demonstrate causation.

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Vandenbroucke observes that some of "those who were wrong" in the smoking-lung cancer debate presented interesting criticisms of the majority view. I must agree with him that their writings deserve study, along with the classics by "those who were right". But I fear that Vandenbroucke may have missed an important distinction between those who were right and those who were wrong, one that divides epidemiologic commentators to this day.

It is my impression that those who were wrong (here, Fisher, Eysenck, and Berkson) would have opposed action against smoking on the grounds that the causal explanation of the smoking-lung cancer association had not been "proven." Their themes are echoed in more recent objections to causal hypotheses with policy implications, such as arguments against the role of aspirin in Reye's syndrome. I believe all those arguments suffer from a philosophical oversight, one with dire medical and public health consequences: All seem to overlook that one can always find noncausal explanations for any observed association, so that the existence of a causal relation is never proved in anything like a mathematical sense. If one adopts a position that action must be forestalled until all plausible noncausal explanations are

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refuted, one will be led to forestall action indefinitely even when the causal explanation is correct.

The consequence of such inaction may be of great cost to health and life. The smoking-lung cancer controversy is a good example. The issue was not, as some misunderstood it, whether the available data proved that smoking caused lung cancer (since it never could). Rather, the issue was (or should have been) whether the available data warranted action. Beyond the scientific data, there was a need to consider the costs of various actions (including inaction) if the causal explanation was correct, the cost of inaction would include a potentially considerable volume of human health and life, along with the attendant medical costs. The costs of action were more purely economic ones, borne primarily by the very industry promoting the risk, but also by society (in the form of lower tax revenues). There was a need to weigh the expected costs of the actions against each other; if these expectations were based on the relative plausibilities of the causal and noncausal explanations, personal judgment would be inescapably involved, since plausibility is subjective. In any case, it seems that by 1959 Cornfield et al. thought that the cost of inaction if the smoking-lung cancer association was causal would so greatly

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exceed the cost of action if the association was noncausal that any reasonable evaluation of the data would dictate action.

Cornfield et al. took care to point out that critics, such as Fisher and Berkson, were not wrong to propose alternative, noncausal explanations for the observed smoking-lung cancer association. Thus, I think the real issue driving the controversy was whether one should equate the stringent criteria for the acceptance of a scientific hypothesis with criteria for making public health decisions. This issue can be discerned in earlier controversies, and it continues to drive current debates. My view is that epidemiologists can afford the luxury of unrestrained scientific skepticism when they function as pure scientists. Some epidemiologists, however, function as public health officials, and others must assist responsible officials (such as the Surgeon General) in making public health decisions. In these public health roles, epidemiologists and the society they serve must recognize the decision to not act as one more potentially wrong and costly decision. This recognition must operate whether the decision concerns the recall of a food product, the regulation of a chemical exposure, the ban of a drug, or simply warning the public

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against a voluntary exposure such as smoking.

When recommending a course of action, one should, of course, recognize that the recommendation may be incorrect. Thus, one should be prepared to continue researching the issue at hand after an action has been taken, at least until scientific consensus has been achieved. For the smoking-cancer relation, it could be argued that criticisms of the causal hypothesis inspire a good deal more research on the relation than might have been conducted otherwise, and that this research sharpened scientific understanding of the relation and provided a basis for further recommendations. As important, though, is that ongoing research makes it possible to discover that an erroneous recommendation is indeed erroneous. Even when later research vindicates a recommendation, it should not blind us to flaws in the earlier research or arguments that led to the recommendations.

To summarize, the issue is not whether those who were wrong produced arguments of scientific interest, for (as Vandenbroucke attests) they did. Rather, the issue is whether they had a complete epidemiologic perspective on their own arguments and the arguments of those who were right. I think not, for issues beyond pure science were at

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stake, public health issues such as the rising incidence of a terrifyingly lethal disease. I ask readers who are skeptical of my thesis to consider whether history would judge those who were wrong as harshly if the disease at issue had been the common cold rather than lung cancer.
(Greenland 1990)

THE AUTHOR REPLIES

Greenland raises interesting and important objections to my treatment of the history of the smoking-lung cancer controversy by moving the discussion to another plane: that of public health action. Thereby, he seems to imply that Fisher, et al. who only looked at the scientific side of the controversy did not really act responsibly, as "complete" epidemiologists should. Perhaps, responsibilities in science and public health have to be divided.

I do agree with Greenland that judgments about causality can never be final. Indeed, many of the writings in Greenland's fine anthology of epidemiologic papers points to the fact that one cannot infer causality once, for always, and for everyone, from data. Causality is, and remains, a subjective judgment in which some views may turn out to be "right" and others "wrong" at a later date. Incidentally, what is

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judged "right or wrong" can also vary with time and fashion: When the science of bacteriology was emerging at the end of the previous century, its proponents judged very harshly on hygiene and miasma theory. Nowadays, we recognize some truth in the latter's objections to bacteriology, i.e., that bacteria cannot be the *sufficient* cause of disease, but that they need other circumstances to flourish. Acceptable truth is variable over time, place, and person.

I also agree that decision analysis will not solve the problem. Imagine a very elementary decision tree on "yes or no action against smoking." If yes, the cost might be putting people out of jobs in tobacco manufacturing. If no, the cost might be premature deaths. One could calculate the cost of both. Next, one should attach probabilities to each of these costs. If the probability of a causal association is judged extremely low, as it was by Fisher, Berkson, and others, the cost of causing unemployment in the tobacco industry will become prohibitive. What decision analysis shows is that the judgment on the causality of the association is crucial. There, the circle closes. This judgment is a scientific one, and certainly a "majority vote" will not do. At what point evidence is sufficient for action should be a matter of concern mainly

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> for politicians and public health administrators, whom scientifically inclined epidemiologists might advise. Politicians and administrators must make decisions in the face of uncertainty. Their decisions require bold courage to make our world a healthier place, based on scientifically uncertain assumptions. Often, however, politicians who have this courage derive it from an unselfish vision of how to shape the world, not from facts. Some beautiful examples of such processes, together with the tobacco-lung cancer controversy, were discussed by Susser. (Vandenbroucke 1990)
>
> (Emphasis supplied; footnotes omitted.)

For legal consideration, what emerges most clearly from these discussions is the crucial distinction between a demonstration of scientific proof of causation -- admittedly lacking -- and a judgment that some public health action is warranted. Unfortunately the 1964 Terry Report and other subsequent resolutions to a large extent discouraged continued critical research. Questioning became unacceptable and condemned. Only by the unfortunate overstatement of proof of causation that has characterized the discussion of the grounds for public health action has the issue been framed in a way that has invited litigation. And, indeed, the Pentti Aho case itself is rooted in an effort to "prove" for public propaganda purposes what cannot be proven scientifically -- thus distorting the role of the courts and abusing the legal system.

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1.4 Earlier Stages

Attacks against tobacco consumption on health grounds are not new; in fact, they go back almost to the time the product was introduced into Europe by the explorers of the Americas. The attacks became particularly vigorous in the United States toward the end of the nineteenth and also in the early years of the twentieth century when cigarettes began to grow in popularity; indeed quite a few U.S. states in that country banned all cigarette sales. Moreover, as the twentieth century progressed, in many nations, including Finland, youths were discouraged in the classroom from using tobacco.

As the Finnish Tobacco Committee (appointed in 1964) stated in its report issued in 1966:

> Those who have opposed smoking have during the entire history of its use regarded it as a health hazard and there have always existed attempts to prohibit or restrict smoking. The understanding of the detrimental health effects of smoking have not, however, been based on sufficient scientific grounds, and indeed it is rather difficult to solve the question for the reason that it must concern human beings and in that context experimental studies are almost impossible.
> (Committee Report 1966:B 69)

The basis for these actions was the universal belief among the public that smoking was harmful for smokers and, indeed, early in the century cigarettes were called "coffin nails" -- a description in use to this day. Nevertheless, by mid-century,

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despite scattered reports in the scientific literature and rarely voiced opinions by a very few doctors, the scientific world did not believe that smoking was causally related to such chronic diseases as lung cancer, cardiovascular and chronic obstructive pulmonary disease.

This mid-century state of knowledge was reflected in lawsuits brought in the United States in the 1950s, when the modern controversy first developed. In Lartigue v. R.J. Reynolds Tobacco Company, 317 F.2d 19, 39-40 (5th Cir. 1963), the appellate court affirmed judgment for defendants, stating:

> Here the manufacturer "had no opportunity to gain knowledge, or to form a judgment as to the dangerous qualities of the product". The manufacturer was in no better position than the consumer.
>
> * * *
>
> Thus far, public policy has not decreed absolute liability for "the harmful effects of which no developed skill or foresight can avoid." At this point, it cannot be said that cigarette smokers who started smoking before the great cancer-smoking debate relied on the tobacco companies' "warranty" that their cigarettes had no carcinogenic element. Today, the manufacturer is not an insurer against the unknowable.

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And in Ross v. Philip Morris & Company, Ltd., 328 F.2d 3, 8 (8th Cir. 1964), the appellate court, in affirming a verdict for defendant, wrote:

> [W]e fail to comprehend how the ends of justice could be served by adopting the fiction that the manufacturer of cigarettes was -- as early as 1934 (when plaintiff began smoking defendant's cigarettes exclusively) -- in a better position, except in theory, than the consumer to ascertain the now highly-publicized causative relationship between smoking and cancer of certain areas of the body. It is perhaps tempting in the light of knowledge of today to create the thought that defendant should have been aware of the cancer-smoking relationship . . . . However, it should be carefully noted that this case must be decided on the facts as they existed in the light of the knowledge of the early 1930s to 1952.

In Green v. American Tobacco Co., 304 F.2d 70, 72 (5th Cir. 1962), after an extensive trial in 1960, a jury in the state of Florida found that prior to the date the smoker's lung cancer was diagnosed, February 1, 1956, the defendant, even with "the reasonable application of human skill and foresight," could not have known that users of its cigarettes would be in danger of contracting cancer of the lung.

In the last half of this century, governments throughout the world have investigated from a public health perspective allegations of disease causation relating to tobacco,

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and many have taken regulatory measures, such as the imposition of warnings, restrictions on advertising, controls of constituents and the like. Following the 1964 Terry Report, the U.S. Congress decided to investigate and legislate as appropriate. Accordingly, extensive Congressional hearings have been held over the years. Those hearings are particularly significant, because dozens of physicians and other scientific investigators publicly stated their views, subject to questioning by members of Congress. A large number testified they did not believe cigarette smoking had been scientifically established as a cause of human disease.

This document relies heavily on the U.S. Congressional hearings, because so much of the early debate had been concentrated around the conclusions of the 1964 Terry Report, not only in the United States but universally, including Finland (cf. Committee Reports 1966:B 69 and 1973:42). These hearings have been a unique forum for the presentation of diverse medical opinions on smoking and health. In addition, this document quotes extensively from leading scientific and medical journals, emphasizing articles whose authors have questioned the smoking-disease hypothesis.

2. CONCEPTS OF CAUSATION IN MEDICAL SCIENCE

Lawsuits, as means of dispute resolution, decide issues between litigants and, after appeal, provide final resolution of

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those issues between the parties. In large measure arising from this finality, concepts of legal causation have stressed the requirements that the cause be a cause-in-fact, i.e., a cause, but for the operation of which the result would not have occurred, and that the cause-in-fact bear legal relationship (see, for example, such concepts as "proximate" and "foreseeability") to the result.

Modern science, in contrast, takes its philosophical roots from David Hume and other empiricists and the intellectual basis for its methods from Francis Bacon (Hume 1730; Bacon 1661). The overview of science is that the accumulation of knowledge is a continuum and, as Vandenbroucke pointed out in the discussion quoted above (Vandenbrouke 1989, 1990), causality is a subjective judgment in which "what is judged 'right or wrong' can also vary with time and fashion."

As Vandenbroucke further points out, politicians and administrators must make decisions in the face of uncertainty. Given the existence of that uncertainty, it is not surprising that the law has provided exceptions in specific contexts (such as the Patient Injury Act and the Occupational Disease Act) where lesser evidence than what normal legal causation criteria would require has been ruled sufficient. (See Suomen Tupakka's brief No. 8 of May 17, 1990, pp. 54-55.) Notably, cases such as this one are not among the exceptions.

The scientific concepts of causation that have developed from Bacon and Hume spring from recognition that

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knowledge is based on inferences derived from observations. Thus, as Hume pointed out, the problem arises because the observation of a sequence of events does not establish with certainty that the same sequence will occur the next time the first event is observed. An example of Hume's point: we infer that the sun will "rise" each morning based upon our observation of that event in the past. If, however, we move our observation post from Helsinki to Lappland in late December, we see that the prediction that the sun will "rise" the next morning is not met. Thus, a correlation of 100% of observations in one place becomes an inadequate basis for prediction in another place.

Moreover, as we know from history, the observations over centuries that the sun "rose" in the east and "set" in the west lead to the inference that the sun circled the earth -- an inference later demonstrated to be exactly the opposite of the truth. And, as the history of science has revealed, Newton's elucidation of the laws of the universe (seemingly capable of validation in all respects except the ability to predict the orbit of the planet Mercury) were fundamentally modified by Einstein's revelations about relativity.

And so science recognizes (or it should recognize) the limitations of inferences based upon observations. It continues to grow by recognizing that today's truth is modified or discarded after tomorrow's discoveries of additional

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information -- a course obviously not available in a court room.

Among other pertinent developments in science, the refinements of experimental criteria as means of validating or invalidating hypotheses stand out. Thus, when scientists began to observe the presence of bacteria in cases where people were ill, they developed what have come to be known as Koch's Postulates (Koch 1884, 1892). These provide an experimental means of testing whether a particular bacteria causes a particular illness. For example, to determine whether the tubercular bacillus causes tuberculosis, the following steps must be taken:

1:0 First, the bacillus is recovered from a diseased individual.

2:0 Then it is introduced into an experimental animal.

3:0 After the animal develops tuberculosis, the bacillus is recovered from that animal.

4:0 It is then introduced into another animal and, after the disease again develops, the bacillus is again recovered.

Only by fulfilling all of these steps is the experiment considered as confirming the tubercular bacillus as the cause of tuberculosis. Thus, Koch's Postulates provide a rigorous basis for testing a causation hypothesis.

Also developed as safeguards against erroneous inferences were the criteria that proposed causal agents must be both <u>necessary</u> and <u>sufficient</u> to produce the result.

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Thus, the tubercular bacillus was viewed as a necessary factor for tuberculosis because the disease did not exist in its absence. It was also viewed as a sufficient factor because its introduction into the test animal produced the disease in virtually every case.

In these ways, then, science has come close to a paradigm for establishing causation by postulating strict experimental criteria and concepts as the bases for validating causal hypotheses. This paradigm works reasonably well for single factor relationships, such as those encountered by science in infectious diseases. Even in such cases, however, complications have developed as, for example, when host factors affect the sufficiency of a causal bacteria.

Much broader complications arise when chronic diseases are encountered. Here, science has gradually recognized that such diseases -- cancer, cardiovascular diseases, pulmonary diseases, arthritic diseases -- will develop in an individual over a considerable portion of the life span. During the past few decades, scientists have observed the correlation of many factors -- both exogenous and endogenous -- with the development of chronic diseases. And so refinements and developments in scientific methods for analyzing etiology have sought to deal with the complications raised by the very nature of these diseases.

The developing science of epidemiology has been one of the principle means utilized for increasing understanding of the

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etiology of these diseases. Since its tools for dealing with etiology are observational and not experimental, epidemiology simply does not have the ability to validate causal inferences by

scientific demonstration. For this reason, the concept of "risk factor" has been developed to describe those factors found by epidemiological observation to be associated or correlated with the occurrence of disease. Risk factors, by their very definition, are not per se causes. They are factors on the scene. They may be causal; they may be indicative of something else that is causal; they may be coincidental; they may be causal in some cases and not in others. Absent other information, any number of statistical manipulations (e.g., multivariate analysis) may assess their significance as risk factors. But no statistical tools exist to establish their significance as causes.

And this was so even in the single factor cases of infectious diseases. For example, in the 19th Century cholera epidemics in England, the correlation of the incidence of the disease and exposure to foul urban air was 100%. And, indeed, the removal of people from the areas where they were exposed to foul urban air produced a virtually complete elimination of cholera. Yet, it became clear that the cholera was transmitted by a contaminated water supply and not by foul air. (Snow 1855; Farr 1885)

An interesting sidelight here: in the interest of justifying action, some epidemiologists have

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argued that Snow's removal of the handle from the water pump was a classic case of disease prevention based upon epidemiological observation when the precise causal agent and the mechanism of disease development were not known. While it is indisputable that cholera was transmitted by exposure to the water, the removal of the handle from the pump,closing off the contaminated water supply, was not the action ending the epidemic. Analysis has shown that the epidemic was naturally on the wane well before the pump handle was removed; the end of the epidemic was a result of the natural course of the disease. The removal of the handle, therefore, is of symbolic and debating importance; it did not, however, demonstrate conclusively the practical results of the application of epidemiology in the absence of full knowledge.

The application of sophisticated epidemiologic techniques, such as case-control studies, has provided additional information in the study of the relationship of various factors to the etiology of chronic diseases. But as Horwitz and Feinstein have demonstrated, even these studies have substantial limitations (Horwitz 1978). Very different magnitudes of risk can appear from the same study population, depending entirely upon the choice of controls to whom the cases are to be compared. Given these and many other methodological limitations, it is not surprising that the debate over the judgments that can and should or cannot and should not be drawn from the epidemiological studies continue, as Greenland admitted, to the present (Greenland 1990).

As the debate has progressed, nuances abound. Thus, some have claimed that epidemiology provides the only means for

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"proving" causation in man but agree that inconsistent experimental evidence may require reevaluation of the conclusions reached. Others, at the other end of the spectrum, view epidemiological evidence with great suspicion and are much more inclined to make or withhold judgment based upon laboratory studies.

MacRae succinctly set forth the limitations of epidemiology in his paper, "What epidemiological studies can tell us." As he concluded:

> We cannot say that everything from an epidemiological study is nonsense, but I hope I have increased your index of suspicion by a relative risk of at least 10.0 that association is not necessarily causation and that sequence is not necessarily consequence. (MacRae 1984)

Not surprisingly, therefore, scientists have long sought to develop experimental means to test hypotheses drawn from epidemiological studies reporting associations or correlations. Scientists have recognized that statistical associations cannot prove cause and effect but, rather, provide information from which hypotheses can be formulated for testing by experimental and other means. The principles involved in formulation of hypotheses and their experimental testing were set forth decades ago by Sir Ronald Fisher, one of the founding fathers of modern statistical theory and of genetics. His essay, Mathematics of a Lady

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Tasting Tea, lucidly explains, in lay terms, such concepts as statistical significance. This essay is attached as Exhibit A.

In laboratory experimentation, confusion is compounded by the fact that laboratory animals do not necessarily develop the same diseases as man and that agents capable of inducing a particular disease in one laboratory animal are not capable of doing so in another. And so, among some scientists, the question is raised as to whether man is more like a mouse or a rat.

Information as to chronic disease etiology has become available from other scientific disciplines as well. Clinical studies elucidate the pathology and course of development of these diseases and cast light upon host factors. Much information is provided by chemical analyses and the development of test mechanisms short of full-scale life studies of animals. Immunology has contributed information about host factors, and concepts of constitutional and genetic contributions to or control of the disease process have been developed as have behavioral and other studies of personality and psychological factors.

The following history of the smoking and health controversy will deal with the accumulation of large amounts of information relating to that controversy, as that information has developed from these various disciplines. Whether the information accumulated at any given date in the past few decades

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is sufficient for public health action is a question that has in fact been addressed and answered by public health authorities. Their conclusions have been various, have sometimes been overstated and have sometimes bordered on zealotry.

But their conclusions are not at issue here. As Greenland has suggested, public health decisions may be based upon assessment of such factors as the impact on public health of acting or not acting on the information available. In a courtroom, however, the law requires -- with exceptions not pertinent here -- far more than inferences attributed to a general population. It requires establishment of legally adequate causation-in-fact in the individual case before the Court. Thus, while the Court may not be in position to resolve the smoking and health controversy, it is in a position to appreciate the significance and limitations of the scientific judgments expressed in that controversy. And, later in the case, in the context of those limitations, we will show that the lack of knowledge of mechanisms and gaps in other crucial information prevent any scientific judgment as to the cause or causes of plaintiff Aho's several disease.

3. EARLY HISTORY OF THE TOBACCO AND HEALTH ISSUE

King James I of England in his 1604 treatise called "A Counterblaste to Tobacco" made the first recorded attack against the product when he branded it as:

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> A custome loathsome to the eye, hatefull to the Nose, harmful to the braine, dangerous to the Lungs, and in the black stinking fume thereof, nearest resembling the horrible Stigian smoak of the pit that is bottomelesse.

In 1615, Shah Abbas of Persia prohibited the use of tobacco in his kingdom out of fear that smoking adversely impacted upon birth rate. The assault continued over many years and in many lands. One of the first visual warning signs that society has considered tobacco to be dangerous to one's health was on the title page of the book "Die Trockene Trunkenheit" (The Dry Intoxication) written by the Jesuit preacher and author Jakob Balden in 1658. The picture which appears on the opposite side requires no explanations. Dr. Bernardino Ramazzini in his treatise entitled Diseases of Workers published in 1700 and revised in 1713 included the following passage about tobacco usage:

> It is not for me to say anything here about the use and abuse of tobacco or to go over the ground again, since the reader can consult Magnen who wrote a special treatise on this subject, and the work of the learned Ettmüller, recently published at Frankfurt with much additional matter, which has a very precise history of tobacco and gives the medicaments that are made with it. All, however, admit that certain unusual disorders

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result from its excessive use, and various statements to this effect are to be found in authors. Helmont, who abhors the habit of smoking, says that he found that the stomach is dyed yellow with tobacco smoke, and he ascribes to it some occult poison. Simon Paulli and Richard Morton add that the lungs are made flaccid and dry by tobacco smoke, and they gradually wither. Or one may read Théophile Bonnet, who describes numerous dissections of corpses from which it appears what serious and horrible injuries to the lungs and brain were found, caused not only by smoking but also by taking snuff. That there is in tobacco great acridity, as in all substances that causes sneezing, is sufficiently proved by the irritation produced in the nostrils by snuff and in the mouth by chewing; also by the poisonous smell that makes the breath of all users of tobacco so offensive. Those who make tobacco, breathe in freely those bad odors and the flying particles of dust which when very fine are correspondingly sharp, so that they prick and dry up the delicate coats of the lungs and trachea. The foul exhalations becloud the animal spirits whose seat is the brain, or rather they deaden them as by narcotic; and at the same time they weaken the acid of the stomach so that they corrupt its fermentation.
(Ramazzini 1964)

In 1798, an American physician, Dr. Benjamin Rush, published an essay entitled "Observations Upon the Influence of

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the Habitual Use of Tobacco Upon Health, Morals and Property."

Similar attacks were echoed during much of the 1800s:

> Smoking and tobacco chewing were harmful to the mouth, stomach, and nervous system, Dr. Rush observed, in addition to being generally filthy and expensive habits. The doctor went on to draw a direct cause-and-effect relationship between tobacco use and drunkenness, a correlation that would persist throughout subsequent anti-smoking campaigns. Dr. Rush was followed by a number of anti-smoking reformers. Dr. Joel Shew, for example, carefully catalogued--often in repellent detail--some eighty-seven maladies directly attributable to tobacco use, including insanity, cancer, and hemorrhoids. The eugenicist Orson L. Fowler believed tobacco possessed certain aphrodisiacal properties--obviously a more damning charge then than it would be today--and warned, "Ye who would be pure in your love-instinct, cast this sensualizing fire from you." The Reverend George Trask, author of the widely circulated 1852 tract "Thoughts and Stories for American Lads" (sub-titled "Uncle Toby's Anti-Tobacco Advice to His Nephew Bill Bruce"), pioneered the misuse of statistics in warning of the dangers of tobacco. "Physicians tell us that twenty thousand or more in our own land are killed by [tobacco] every year," Trask wrote in 1859. "German physicians tell us that of deaths of men between the ages of eighteen and twenty-five, one-half originate from this source." Joining in the ante-bellum anti-smoking campaign were such men as Horace

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Greeley (who described a "long nine" cigar as, "a fire at one end and a fool at the other"), Henry Ward Beecher, and even P.T. Barnum.

* * *

In the 1880s and 1890s the cigarette's effects on smokers were thought to be not only immediate and debilitating but also often fatal. Consider the following case, as reported by The New York Times in 1890.

CIGARETTE SMOKING KILLED HIM

New Jersey--The death of eight-year-old Willie Major, a farmer's son, from excessive cigarette smoking is reported from Bound Brook. The boy had for over three years been a victim to the habit. He would stay away from home several days at a time, eating nothing but the herbs and berries of the neighborhood and smoking constantly. Sunday he became ill and delirious. He died Tuesday in frightful convulsions.

There were dozens, perhaps hundreds, of similar case histories.

Even if death did not immediately claim the young smoker, failing health surely would. Among the maladies attributed to cigarette smoking were color blindness, "tobacco amblyopia" (a weakening of the eyesight), baldness, stunted growth, insanity, sterility, drunkenness, impotence (or

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> sexual promiscuity, depending on the point to be made), mustaches on women, and that traditional bugaboo of nineteenth-century America, constipation. No less alarming was the moral dissipation caused by cigarettes, a process cogently described by New York school commissioner Charles Hubbell in 1893: "Many and many a bright lad has had his will power weakened, his moral principle sapped, his nervous system wrecked, and his whole life spoiled before he is seventeen years old by the detestable cigarette. The 'cigarette fiend' in time becomes a liar and a thief. He will commit petty thefts to get money to feed his insatiable appetite for nicotine. He lies to his parents, his teachers, and his best friends. He neglects his studies and, narcotized by nicotine, sits at his desk half stupefied, his desire for work, his ambition, dulled if not dead." (Dillow 1981)

The nineteenth century painter Vincent Van Gogh was a smoker. A famous painting of a skull with a cigarette, thought to have been done in 1886, copied on the opposite side, is said to be a self-portrait. He once wrote to his brother that he was smoking a great deal and had a cough productive of a grayish phlegm. (Carr 1989)

At the close of the nineteenth century and early in the twentieth, cigarette sales were banned for health reasons in a number of states in the U.S. For example, a statute adopted by the legislature of the state of Tennessee in 1897 provided:

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Skull with Burning Cigarette
Antwerp, Winter 1883–86
Oil on canvas [illegible] cm

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> [I]t shall be a misdemeanor for any person, firm, or corporation to sell, offer to sell, or to bring into the State for the purpose of selling, giving away, or otherwise disposing of, any cigarettes, cigarette paper, or substitute for the same; and a violation of any of the provisions of this Act shall be a misdemeanor, punishable by a fine of not less than fifty dollars.
> (Tennessee Acts 1897)

In upholding the validity of the legislation, the Tennessee Supreme Court observed:

> Are cigarettes legitimate articles of commerce? We think they are not, because wholly noxious and deleterious to health. Their use is always harmful; never beneficial. They possess no virtue, but are inherently bad, and bad only. They find no true commendation for merit or usefulness in any sphere. On the contrary, they are widely condemned as pernicious altogether. Beyond question, their every tendency is toward the impairment of physical health and mental vigor. There is no proof in the record as to the character of cigarettes, yet their character is so well and so generally known to be that stated above, that the Courts are authorized to take judicial cognizance of the fact.
> (Austin v. Tennessee, 1900)

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In World War I, United States troops marched to a song that contained the following lines:

> Ashes to ashes and dust to dust,
> If the Camels don't get you,
> The Fatimas must.
> (Carr 1989)

And, around 1920, a character in the classic Sinclair Lewis novel, "Main Street", said that staying in the village of Gopher Prairie was "more dangerous than the cancer that will certainly get me at fifty unless I stop this smoking." (Carr 1989)

Throughout the first half of the twentieth century, many youth oriented publications throughout the world, including school textbooks and scout manuals, warned their readers against claimed adverse health effects of tobacco use. For example, in 1921 the World Book Company's textbook of Physiology, Hygiene and Sanitation entitled, The Human Body And Its Enemies asserted:

> Doctors speak of an "alcohol heart" and a "tobacco heart": an unsteady, palpitating, fluttering, unreliable heart. Tobacco is particularly harmful to the young boy of grammar or high school age. At that time the heart grows rapidly and any interference with its proper development is sure to lead to permanent injury.
> (Hartman 1921)

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In 1928, the Finnish textbook by K.E. Kivirikko entitled, Primary School Natural History (3rd edition) stated:

> Tobacco contains above all a poison called nicotine, but there are many poisonous gases in tobacco smoke. The poisonous effects of tobacco appear at the best in persons, who only begin to smoke: the face gets pale, the body is covered by cold sweat, the pupillary contract, the ears ring and the head aches. He also feels sick (vomiting) and dizzy, he has accordingly become sick. The first smoking can even result in death. But what about those pains, it is manly to smoke, think many young boys.
>
> One can get used to anything, even smoking. Many take a liking for being quite sick, unless they continuously can suck poisonous gas into his lungs. The body seems to be able to stand the poison of tobacco very well. But it is quite clear that if a strong poison kills, then even a mild poison in small doses continuously taken causes disturbances in the function of the organs. Sooner or later the smoker becomes poisoned by nicotine however resistant his body may be. The smoker becomes a slave of his lusts, he has difficulties in giving up his tobacco. From the poisoning finally even the hands start shaking, the function of the heart gets weak. The breathing and digestion organs do not function regularly, and the arteries start to harden (calcify) too early. When calcifying, the walls of the arteries become

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hard and brittle. Even from sneezing such an artery may rupture which results in hemorrhage and apoplexy. Also the artery, which transports nutrition to the muscles of the heart gets calcified often also from nicotine. It hardens, becomes too narrow and can no longer sufficiently nourish the heart with the result that it stops functioning.

The poisonous effect of tobacco does not only reduce the working capacity of the body, but it can also prevent its development. Tobacco has a much more destructive effect on children than on adults. Many smokers stay persistently thin, but if they for a while can give up that ugly and untidy habit, they already start to show signs of putting on weight. This also shows that tobacco disturbs digestion.

Tobacco also reduces resistance against infectious diseases. The workers of the tobacco manufacturers get in astonishingly great numbers lung disease(s) and die prematurely. The tobacco makers' children are weak and pale and succumb to a premature death.

In addition it should be noted that hundreds of million Finnmarks are annually wasted on tobacco in poor Finland. In many households smoking means quite big sums which could have been used in many ways for the benefit of the home and in particular the children.
(Kivirikko 1928)

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An extensive condemnation of tobacco use was set out in the 1929 Ginn and Company textbook entitled Science And The Way To Health:

Tobacco injurious to young people

There may be a difference of opinion as to the effects of tobacco on adults, but there is general agreement that its use is dangerous to children and young people. There are at least four reasons for this agreement.

First of all, youth is the time for growth. There is a general belief that tobacco interferes with physical development. Dr. Boas, in his study of 45,151 boys, found that those who smoked were, on the average 1.13 inches shorter than they should be for their age, and the non-smokers were 2 inches taller than the average. In weight the difference was 7.1 pounds in favor of the nonsmokers. Since tobacco is a narcotic and not a food, this is what might be expected.

Second, tobacco, like alcohol, is habit-forming. Some find it impossible to break the habit, or, if they do, they experience real distress. Many people become so addicted to the use of tobacco that if they cannot get it they are very irritable and unhappy. Some cigarette-users become so nervous and uneasy

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that when in a social group where smoking is forbidden they feel compelled to excuse themselves. At that point the craving for tobacco has become stronger than mind or will power.

Third, most young people cannot afford to spend their money for such a luxury. Often they feel that they do not have enough money to spend. They should be saving to get more education or to start in business. The wise youth will spend money where it will count most.

Fourth, there is little doubt that tobacco affects scholarship and skill. Professor Frederick J. Pack studied the scholarship of university men, in six different institutions, who tried to make the football team. This is what he found:

1. Only half as many smokers as nonsmokers are successful in the "try-outs" for football squads.

2. In the case of able-bodied men, smoking is associated with loss of lung capacity amounting to approximately 10 per cent.

3. Smoking is invariably associated with low scholarship.

(Andress 1929)

A similar theme was voiced in the 1933 Ginn and Company textbook entitled Health And Good Citizenship:

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Here are some of the principal reasons why smoking is bad for young people:

1. Smoking tends to stunt growth.

2. Tobacco smoke is always an irritant to the mouth, throat, and lungs.

3. Tobacco is harmful for athletes.

4. The use of tobacco often leads to a disregard for ordinary politeness. Smokers sometimes use tobacco in the presence of those who find tobacco smoke very offensive.

5. The use of tobacco in any form is expensive.

6. The habit is a luxury, since it is quite unnecessary.

7. When the tobacco habit is once formed, it is hard to break. The smoker is likely to become its servant and slave.

(Andress 1933)

The Finnish textbook by Kaarin Kari and K.U. Suomela, Hygienics for High School, of which several editions were published in the 1930s and 1940s warned that:

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> Tobacco smoking damages the lungs both with the nicotine and also with other substances it contains . . . .
>
> * * *
>
> Tobacco contains an oily alkaloid called nicotine which simply is a very strong poison and the quantity of which in some tobacco brands can be as high as 4%. The highest quantity of nicotine gets into the body by chewing tobacco. But although by smoking only a part of the nicotine in the tobacco gets into the body, in addition thereto the smoker will, however, draw into his lungs many other poisonous substances which develop in the tobacco smoking (for example picoline and pyridine alkalines, carbon oxide, hydrocyanic acid etc.).
> (Kari-Suomela 1943)

Please be reminded that the textbooks of Kari and Suomela and of Kivirikko were also plaintiff Pentti Aho's school books.

4. THE LUNG CANCER CONTROVERSY

4.1 Early History

In the last few decades, the primary focus of the tobacco/health controversy has been on lung cancer. It has been fueled by a claim that cancer of the lung has had an increase paralleling the growth in cigarette

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consumption. However, a number of medical scholars has demonstrated that lung cancer has plagued mankind for hundreds of years, that such increase as may have occurred began in the nineteenth century (before cigarette smoking became popular), and that the reported increase is more apparent than real. For example, Dr. R.H. Rigdon, Professor of Pathology at the University of Texas School of Medicine, presented an historical analysis in June 1956, and in July 1957 which was reported in the transcript of hearings held before a Subcommittee of the Committee on Government Operations, U.S. House of Representatives. (U.S. Congress, House of Representatives, Subcommittee of the Committee on Government Operations, False and Misleading (Filter-Tip Cigarettes): Hearings, 85th Cong., 1st sess., 18-19; 23-26 July 1957. Hereinafter cited as "H.R. 1957".)

After having reviewed the early history of lung cancer from Agricola's findings of lung cancers in miners in 1921-1927 to Adler's report in 1912, he quotes Sweany who in 1934 stated, "During the last half century primary lung cancer has sprung from obscurity into a rather common disease." Rigdon paraphrased Sweany's conclusions that,

> part or perhaps much of this increase may be attributed to: (1) an increase in life expectancy; (2) increased knowledge in the course of certain diseases such as tuberculosis and bronchiectasis;

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(3) the tremendous effect on diagnosis brought about by the x-ray and the bronchoscope; (4) increased zeal on the part of the medical profession and laity as indicated by better hospitalization and better transportation; and (5) the changing attitude in the pathologic interpretation of lung cancer referable to metastases and sarcoma.

* * *

Rigdon added:

Time does not permit a discussion of the many agents which have been suggested as the etiology of lung cancer. Among those considered have been tuberculosis (Ewing 1928), syphilis (Pilot 1927), influenza (Berblinger 1925), diphtheria and measles (McKenzie 1907), chronic pulmonary inflammation (Duguid 1927), pulmonary scarring (Wolf 1895), road dust (Simons 1937), dust from grooming horses (Hudson 1926-1927), motor exhaust (Morse 1945), war gas (Brockbank 1932), cigar makers and sorters (Brinkman cited by Simons 1937), arsenic (Neubauer 1947) chromium (U.S. Pub. Health Serv. 1953), asbestosis (Lynch 1935), silicosis (Fine 1935), metaplasia (Katz 1927), tar (Probst 1927), heredity (Schwyter 1928), trauma (Wells 1930) air pollution (Mills 1953), cigarette smoking (Wynder 1950) and inhalation of printers ink while reading the morning newspaper. (Ask-Upmark 1955)

The history of the cigarette-cancer causation theory includes a complete reversal of opinion in 1948 by Dr. Alton Ochsner, a noted U.S. surgeon, who had once been,

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then recanted, and then later again became, one of the most outspoken opponents of tobacco use in the world. (Ochsner 1948) Indeed, that same year, The Journal of the American Medical Association published the following editorial statement regarding cigarettes and health:

> For some years The Journal of the American Medical Association, the state medical journals and most other medical publications have carried the advertisements of the various companies that manufacture cigarettes. Actual surveys indicate that the majority of physicians themselves smoke cigarettes. Extensive scientific studies have proved that smoking in moderation by those for whom tobacco is not specifically contraindicated does not appreciably shorten life. Postmortem examinations do not reveal lesions in any number of cases that could be definitely traced to the smoking of cigarettes. From a psychologic point of view, in all probability more can be said in behalf of smoking as a form of escape from tension than against it. Several scientific works have been published that have assembled the evidence for and against smoking, and there does not seem to be any preponderance of evidence that would indicate the abolition of the use of tobacco as a substance contrary to the public health.
> (J.A.M.A., 1948)

Moreover, as Dr. Matti Rimpela has observed (and even though, for example, Professor Rauramo had implicated smoking in

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his 1942 inaugural address at the University of Helsinki and the Finnish Cancer Society had discussed the health risks associated with smoking in 1949), the claimed health hazards of tobacco were not emphasized by the international medical community during this period:

> [O]ne cannot help but ask why the health hazards of tobacco were not stressed by the medical establishment to a larger extent before the 1950s. The first evidence of its damage, after all, had already been presented much earlier. As an example of this delay, we can point to the review article by Vaino Kannisto, which was published in Doudecim in 1951, where he writes about the reasons for the excessive death rate among Finnish men. At that time Kannisto served as an epidemiologist at the World Health Organization headquarters and his point of view represented the best professional opinion of the time. Kannisto debates the relative contributions to the excess death rate of such factors as working and living conditions, rheumatoid arthritis, syphilis and alcoholism, but he does not even mention tobacco. (Rimpela 1975)

In a volume of the Journal of the American Medical Association which appeared the same year (1948) Dr. Edward Churchill, Professor of Surgery at Harvard University, published a "Special Article" on behalf of the American Medical Association and in cooperation with the American Cancer Society, entitled "Primary Carcinoma of the Lung." In discussing "prevention," Dr. Churchill warned against relying upon "speculations" to prove that cigarette smoking was a cause of disease and concluded that there was still "no factual evidence" of such a relationship. He continued:

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> Nothing is known about the cause of the disease that can be translated into effective preventive measures. It is possible that an actual increase in the incidence of pulmonary cancer has taken place during the first half of this century. Several statistical studies support such an interpretation. On the other hand, Boyd (footnote omitted), who is in a position to speak freely of the shortcomings of pathologists, thinks the disease was not recognized twenty years ago because it was not looked for. At any rate, evidence that pulmonary cancer was on the increase led to several speculations about causative agents, and among other things, cigarette smoking was incriminated. Further knowledge about the nature and the mode of action of carcinogenic agents, and a careful recording of the smoking habits of ample numbers of patients with the disease, provide no factual evidence on which advice to give up smoking for this reason can be based.
> (Churchill 1948)

4.2. Development Of The Modern Controversy

Wynder and Graham reported in the May 27, 1950 issue of the Journal of the American Medical Association the results of a retrospective study of over 600 lung cancer patients and an equal number of controls which concluded that "excessive and prolonged use of tobacco, especially cigarettes, seems to be an important factor in the induction of bronchiogenic carcinoma." (Wynder 1950)

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In September 1950, the British Medical Journal published a "Preliminary Report" of a retrospective study conducted by Doll and Hill which stated:

> [T]here is a real association between carcinoma of the lung and smoking. Further, the comparison of the smoking habits of patients in different disease groups, shown in Table X revealed no association between smoking and other respiratory diseases or between smoking and cancer of the other sites (mainly stomach and large bowel). The association therefore seems to be specific to carcinoma of the lung. This is not necessarily to say that smoking causes carcinoma of the lung.
> (Doll 1950)

In 1952, Doll and Hill reported an analysis of a much larger number of lung cancer cases. This later report concluded:

> that the association between smoking and carcinoma of the lung is real. It is not argued that tobacco smoke contributes to the development of all cases of the disease -- a most unlikely event. It is not argued that
>
> it is the sole cause of the increased death rate of recent years nor that it can wholly explain the different mortality rates between town and country.
> (Doll 1952)

The distinguished professor of experimental pathology at The University of Leeds, Dr. R.D. Passey, criticized the findings of Doll and Hill, and made the following observation:

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> It may be that a proportion of lung cancers in man are induced by tobacco smoke: at the moment we do not know, but let us be sure of our evidence before we scare our public. As a profession we have that responsibility.
> (Passey 1953)

In mid-1953, a lead article by Dr. D.W. Smithers, Director of the Radiotherapy Department of the Royal Cancer Hospital, London, was published in the British Medical Journal. The article included the following comments:

> The moment the word cancer is mentioned to the public (of which doctors are but a part) emotion is aroused and any calm objective view of the value of evidence presented becomes most difficult. It is important that the medical profession take note of this difficult problem of lung cancer and help to deal with it more efficiently, but it is also important that they do not make matters worse by merely joining in a cry and increasing the alarm. A sensible view of the relationship of smoking to this problem, for instance, should be and, after some wild comments in the lay and medical press, is now being presented to the general public; but no comparable effort seems to be going into an endeavor to persuade the authorities to cleanse the air of our industrial towns. As a profession which speaks so much and so rightly of the need to allay the cancer fear

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> we should be aware of putting extravagant accounts of rising cancer death rates and their causes before the public, especially when neither the magnitude of the one nor the degree or responsibility of the other has yet been fully established.
> (Smithers 1953)

In the December 1953 issue of Cancer Research, Wynder and Graham presented the results of an experiment conducted by painting cigarette "tar" on the backs of a laboratory species of mice. They concluded that "condensed cigarette tar [was established] as a carcinogen for mouse epidermis." They observed:

> These studies provide a tool to determine and isolate the possible carcinogenic agent(s) within tobacco tar. At present it is not known which fraction or fractions in tobacco tars are carcinogenic. Combined chemical and biologic studies are now in progress to search for such agents. Such studies, in view of the corollary clinical data relating smoking to various types of cancer, appear urgent. They may result not only in furthering our knowledge of carcinogenesis, but in promoting some practical aspects of cancer prevention.
> (Wynder 1953)

The Wynder and Graham paper had to be weighed in the light of a book published by the National Cancer Institute of the United States Department of Health, Education and Welfare in 1951

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entitled "Survey Of Compounds Which Have Been Tested For Carcinogenic Activity." In the Introduction of that work, a number of "pitfalls in the use of a survey like this to affirm or deny a proposed theory of carcinogenesis" were discussed, including the following:

> Furthermore, in the mouse itself, it is now abundantly evident that different tissues respond differently to the same compound. Some compounds have given negative results when applied to the skin but have been quite active when injected subcutaneously. With other compounds both techniques have given positive results but have brought out pronounced differences in the response of the skin and of the subcutaneous tissue. Compounds that are potent for the skin and subcutaneous tissue were found to be inactive when introduced directly into the liver. . . The susceptibility of the lungs. . . does not necessarily parallel that of the skin or the subcutaneous tissue.
>
> * * *
>
> Another pitfall is the attempt to carryover, without reservation, to man, conclusions based on animal experiments. We do not know whether man is more or less susceptible than mice to particular carcinogens. Some animal species, such as the rat, rabbit and dog, are much more resistant to certain chemical carcinogens than is the mouse, and vice versa, while in the monkey none of the powerful carcinogens has been shown to produce tumors. It would, therefore,

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> be dangerous to conclude that man is resistant or susceptible to a given carcinogen merely on the basis of experiments with a single species of laboratory animal since we also know of several chemical agents which, as occupational hazards, are responsible for some human cancer and which have so far yielded negative results in laboratory animals.
> (U.S. PHS 1951)

E. Cuyler Hammond, who was the director of the statistical research section of the American Cancer Society stated his position about the nature of the relationship between smoking and lung cancer at the Society's annual meeting on November 3, 1953. He concluded that there were three possible factors to consider with respect to the rise in lung cancer -- cigarette smoking, automobile exhaust fumes and pollution from coal and oil furnaces. He concluded that "the full facts are not yet known about any of these possible factors" and warned that premature conclusions about any one factor would stifle important research. With respect to cigarette smoking he found that "the degree of influence of cigarette smoking as the causation of lung cancer is still an open question."

> From what we know at present, there are at least three different environmental factors and probably more that could be at least partly responsible for the rise in lung cancer: (1) cigarette smoking; (2) exhaust fumes from automobiles; and (3) air pollution

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from coal and oil furnaces. All of these contain substances that can produce tumors in experimental animals. All three come into direct contact with the lung. All three affect a very large proportion of the population. The first two, and to some extent the third, have been increasing during the period in which lung-cancer death rates have been rising. The last two, automobile fumes and general air pollution, are heaviest in urban areas, and reported death rates from lung cancer are higher in urban areas than in rural areas. Whether cigarette smoking is also heavier in urban areas than in rural areas in the United States is somewhat uncertain, but this will be known before long. Wynder said it is so in England.

In my opinion, the full facts are not yet known about any of these possible factors. Some investigators have expressed the opinion that, while cigarette smoking may not be the only cause of lung cancer, it is at least by far the most important cause and accounts for the increase in the death rate. If this view is now accepted as fact, it inevitably will have the result of reducing research in respect to other possible causes. After all, you cannot expect the public to put up millions of dollars for investigation of other possibilities if everyone thinks the answer has been found. For this reason, if for no other, I should want very strong proof indeed before I would be willing to state as

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an absolute fact that I know cigarettes to be responsible.

* * *

Laboratory investigations of the chemical composition of tobacco smoke and of the effect of smoke and smoke distillates on experimental animals have not so far yielded very much definitive information of a convincing nature concerning the causes of lung cancer in the human population.

* * *

In my opinion, the degree of influence of cigarette smoking as the causation of lung cancer is still an open question.

* * *

All of the studies of smoking in relation to human lung cancer previously described by Wynder were based on the backward method of approach, although the exact details vary. Because of the known difficulties with this method, certain investigators, including myself, are not completely convinced as to the validity of the results, in spite of the fact that a number of independent studies conducted in more or less the same way led to more or less the same apparent conclusions.

* * *

Although it may turn out that smoking is relatively harmless, yet considering their enormous financial stake in the matter, to say nothing of their moral obligation, it would seem sheer stupidity if both the Government and the tobacco companies do not immediately give strong financial backing to research into possible harmful ingredients in

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> cigarettes and ways of removing them if such are found. In all justice, at least a tiny fraction of the gigantic tax on tobacco might be devoted to this purpose.
>
> I will close with one other suggestion. Unless and until it is proved that smoking is the only culprit, we must not neglect research on the other possible causative agents.
> (Hammond 1954)

In January 1954, W.C. Hueper of the United States National Cancer Institute, after providing a detailed analysis of the leading smoking/cancer literature, concluded that the available evidence did not prove and, moreover, did not even "strongly indicate" that cigarette smoking was a major cause of lung cancer. In support of his skepticism, he noted, for example, that the rise in lung cancer preceded the adoption of cigarette smoking by two decades, that there were substantial differences in lung cancer rates between rural and urban areas and that lung cancer rates varied between areas with similar environments.

> One may develop, moreover, some doubts as to the medical validity of the statistical data advanced in support of the cigarette theory, if one contemplates the fact that Doll did not find a positive association of respiratory irritative symptoms for individuals with cancer of the lung, although

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the prevalence of a chronic cough, i.e., 'the cigarette cough,' is a well recognized clinical manifestation in chain smokers.

In clinically evaluating the claims made in regard to the predominant origin of lung cancer from excessive cigarette smoking, it may be well to remember that the start in the rise in lung cancer incidence occurred around the turn of the century and therefore preceded by about two decades the widespread adoption of the cigarette smoking habit. This fact deserves serious consideration because various investigators have given a latent period of 20 to 40 years for cigarette cancer of the lung.

The existence of consistently and markedly higher incidence rates of lung cancer for populations residing in industrialized and urbanized regions in comparison to those found for rural populations by English, Danish, German and American investigators, as well as of considerable variations in lung cancer morbidity rates established by recent studies of American workers for population groups of similar environmental background (metropolitan areas of 10 American cities), must deepen the suspicion that other and apparently more important environmental factors than cigarette smoking are causally related to the causation of lung cancer and its alarming rise in incidence.

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> It may be concluded that the existing evidence neither proves nor strongly indicates that tobacco smoking, and especially cigarette smoking, represents a major or even predominating causal factor in the production of cancers of the respiratory tract and are the main reason for the phenomenal increase of pulmonary tumors during recent decades. If excessive smoking actually plays a role in the production of lung cancer, it seems to be a minor one if judged from the evidence on hand. However, it may be well to remember in this connection, the concluding statement of Doll and Kennaway, that "the study of the relation between the national consumption of tobacco and the national incidence of cancer of the lung has scarcely begun."
> (Hueper 1954)

In June 1954, Drs. Curwen and Kennaway, of the Pathological and Statistical Departments of St. Bartholomew's Hospital, London, published an in-depth report on the incidence of lung and larynx cancers in England and Wales during the period 1921-1951. While it was noted that there had been a large increase in the number of deaths ascribed to lung cancer in that period, there had been little change in the number of reported laryngeal cancers, notwithstanding an increase in population. The authors commented as follows:

> Two main points have emerged from this analysis: first that many of the differences that can be detected in the mortality due to cancer of the lung and larynx between one part of the country and another are due to differences in the level of urbanization.

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> Whether this applies to all the differences we cannot yet say; in particular there is a suggestion that other factors may be at work in Wales. The second point is that the exact form that this association takes is not the same in men as in women. For cancer of the female lung the urbanization gradient is less steep than in males, though both are positive; for the larynx the slope is positive in males and negative in females. These facts are clearly relevant in the search for the cause or causes of these forms of cancer, whether this be smoking, atmospheric pollution, or some occupational or social factor.
> (Curwen 1954)

In July of that year, the Reader's Digest, the most popular magazine in the United States, published an article entitled, "The Facts Behind The Cigarette Controversy," which discussed much of the leading literature that had been published up to that time regarding smoking and possible disease causation. (Miller 1954) Between 1950 and 1954, Reader's Digest (Valitut Palat) had published four articles in Finland dealing with tobacco. Each of the articles presented information on the health risks associated with cigarette smoking. The titles and dates of publication are set forth below.

January 1950:	Thank You, I Don't Smoke
February 1953:	Tobacco Causes Cancer
February 1954:	Can One Smoke Without Risk?
August 1954:	Cigarettes and Lung Cancer

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Hammond and Horn, on behalf of the American Cancer Society, reported on the "Relationship Between Smoking Habits and Health Rates" in an August 1954 issue of the Journal of the American Medical Association. (Hammond 1954) A condensed version of the paper had been read at a meeting of the American Medical Association on June 21, 1954. The major findings were that (1) the death rate of cigarette smokers was far higher than the death rate of men who had never smoked cigarettes, and (2) deaths ascribed to cancer accounted for about one-quarter of the excess deaths among cigarette smokers, while deaths ascribed to coronary artery disease accounted for over one-half the excess.

The New York Times reported the Hammond and Horn findings in its June 27, 1954 edition. It noted that "the American Cancer Society does not say this 'proves' that cigarette smoking causes cancer. Some authorities noted the possibility that certain glandular imbalances which might predispose a man to smoke conceivably might also predispose him to these diseases." (N.Y. Times 1954)

In 1956, the British Empire Cancer Campaign published its 33rd Annual Report. As in previous years, the Campaign was chaired by a panel of distinguished scientists and lay persons. Its Scientific Advisory Committee was jointly appointed by The British Royal Society, The Medical Research Council and The British Empire Cancer Campaign.

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In its discussion of research into "Tobacco Smoking and Atmospheric Pollution in Relation to Lung Cancer," the Report described the negative results of the experimental efforts to produce lung cancer in animals with cigarette smoke.

> Attempts have been made to produce cancer in the lung of rats by the direct injection of tobacco tar and also of various carcinogens into the lung. At another centre cigarette smoke tar and resin have been injected into the lungs of mice; the few tumours that developed were regarded as spontaneous and in no way due to the effect of the injected material.
>
> Experiments set up to test for carcinogenicity in cigarette tar by its application to the skin of the mouse have now been completed, with negative results. No malignant tumours were obtained either with the whole tar or with the neutral fraction. Nor have any tumours as yet appeared in rats injected subcutaneously with fresh cigarette tar, or hamsters which had cigarettes made entirely from cigarette paper have shown no tumours yet. In other experiments to test crude tars condensed from cigarette smoke, no skin tumours were obtained in mice painted twice weekly with a 20 per cent solution of the tar in acetone. Using still another route, at another centre, tar obtained in a

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smoking machine was introduced into the oesophagus of mice, a route of administration which has given a high yield of lung cancer after the introduction of a known carcinogen; no definite carcinoma of the lung has developed to date.
(British Emp. Cancer Campaign 1956)

Also in 1956, in a book written by Dr. Charles S. Cameron, the Medical and Scientific Director of the American Cancer Society, entitled "The Truth About Cancer", the author discussed the possibility that the statistical association between smoking and lung cancer was an incidental result of the tendency to smoke and the tendency to get lung cancer, with both being influenced by hormonal factors.

> The question uppermost in the minds of scientists at the moment is whether the well-established and generally accepted statistical association between cigarette-smoking and cancer of the lung is one of cause and effect, or whether it is incidental. It is possible that the tendency to smoke heavily and the tendency to get lung cancer are both the result of a common and as yet unidentified factor or cause. One such influence might be a distinctive type of hormone balance. It is known that hormones seem to be involved in the development of certain kinds of cancer, and it is conceivable, though far from proved, that the hormone stimulation may be responsible for a high pace of living, carrying with it an intense desire to smoke.

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> Explanations like this are pure speculation, but ways are being sought to put them to the scientific test. The final answer will probably be years in coming. (Cameron 1956)

In the first part of 1957, the American Cancer Society organized a scientific committee which held a series of six, two-day meetings to review data in the area of cigarette smoking and lung cancer. The committee issued a report which appeared in the June 7, 1957 issue of Science. (Shimkin 1957) According to Dr. Michael B. Shimkin, who was Director of Field Studies* of the National Cancer Institute, the report had little impact and was not generally accepted as convincing. Shimkin also observed that the chiefs of the laboratories at the National Cancer Institute, including the epidemiologists, were skeptical about the claimed link between smoking and lung cancer.

> . . .[the report] created no particular stir and was not accepted as sufficiently convincing by either the National Heart Institute or the American Heart Association. I recall a conversation with the Director of the National Heart Institute,

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* "Field Studies" encompassed epidemiology, biometry, environmental carcinogenesis and diagnostic research branches of the National Cancer Institute.

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> who dismissed the report with a flip remark. The NCI, however, was doing not much better. Heller [the Director of the National Cancer Institute] gathered his laboratory chiefs and received more denials than support. Dr. M.J. Shear, an expert on carcinogenesis, and Dr. Harold L. Stewart, the head pathologist, refused to recognize epidemiologic data that were not confirmed in laboratory animals. Dr. Wilhelm C. Hueper thought that occupational causes of lung cancer were of greater importance and needed public health controls more than a social habit that represented individual choice. Even the epidemiologists, with Gilliam in the lead, voiced more doubts. Thus, no consensus of scientific opinion was available for Heller to present to his superiors. (Shimkin 1979)

On July 12, 1957, the U.S. Public Health Service released its next proclamation on tobacco use and cancer, along with a statement of the then Surgeon General, Dr. Leroy E. Burney. The release stated in part:

> In today's statement Dr. Burney said many independent studies have confirmed beyond reasonable doubt that there is a high degree of statistical association between lung cancer and heavy and prolonged cigarette smoking.

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Although this evidence is still largely statistical in nature, Dr. Burney said, some laboratory studies also support the concept of a cause and effect relationship.

Dr. Burney noted that many important public health advances have been developed on the basis of statistical or epidemiological information.

Copies of the Surgeon General's statement, together with supplementary data, will be made available to State health officers and others in the health professions as a further step in bringing the matter of smoking and lung cancer to public attention.

Dr. Burney said it is clear that cigarette smoking is not the only causative factor in lung cancer. Further, he said, the precise factors in cigarette smoking which can cause lung cancer are not known.

He said more research is needed to identify and try to eliminate these factors. He also called for more research into other probable causes of lung cancer, including air pollution.
(Burney - H.R. 1957)

In a presentation to the House of Representatives Subcommittee in July 1957, Surgeon General Burney recognized that further

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research was needed "on the question of tobacco and its relationship to lung cancer."

> It is apparent that further research, both on the general question of tobacco and its relationship to lung cancer, and on the question of filtration or other means of modifying cigarettes, is needed. The Public Health Service is prepared, of course, to play its part in this research, of importance to industry, to our economy, and to the health needs of the people of the Nation. (Burney - H.R. 1957)

At the same hearings a number of distinguished scientists testified that the causal relationship between cigarette smoking and disease had not been proved. For example, Dr. Ian Macdonald who was Clinical Professor of Surgery at the University of Southern California School of Medicine and a member of the National Board of Directors of the American Cancer Society concluded that a causal relationship had not been established. He was especially impressed by the fact that animal experiments had failed to confirm the claimed causal relationship.

> One must say that there is an apparent association between cigarette smoking and lung cancer, but when one reviews the total evidence, I think it is not possible to establish a cause and effect relationship.

* * *

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Now, the cause of lung cancer must be much more complicated than the oversimplified thesis of cigarette smoking. . . .

Still another curious finding advanced by the advocates of cigarette smoking in relation to lung cancer is the fact that the dilution of cigarette smoking by some use of cigars and pipes materially decreases the probability or the risk of lung cancer. This seems to be without reference to the degree of moderation or excessiveness with which the individual uses cigarettes along with cigar and/or pipe. If cigarettes are carcinogenic they surely should be so whether accompanied by tobacco in other forms or not. It is an insult, I think, to reason, to believe that two men who indulge equally in cigarettes will have a different chance of lung cancer simply because one periodically adds to his cigarette smoking the use of tobacco in another form.

* * *

Several studies have demonstrated a relationship in social and economic status and lung cancer and I am inclined to think that this factor is of some real importance.

In New Haven, Connecticut, for example, Cohart reported the incidence of lung cancer was more than 40 percent greater among the poor than among the more fortunate economic

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groups. Cohart concluded that unless one could assume that cigarette smoking is inversely related to economic status -- and this seems to be an unjustifiable assumption -- it is reasonable to conclude that important environmental factors other than cigarettes are contributory.

* * *

Differences in lung cancer rates in the country and in the city are consistently found. Several investigators have concluded that residence and employment in urban areas with constantly increasing industrialization constitute more significant and reasonable associations with lung cancer than smoking.

* * *

Still further, mice and men are completely unlike in their response or lack of response to many agents. . . . I think it is proper, therefore, to make these generalizations on this subject.

(1) The demonstration of the production of cancer by an agent in a mouse cannot be accepted as valid evidence of a similar property in men, particularly if the experiment cannot be repeated successfully in the higher mammals, which has certainly not been done in the instance of tobacco tars.

(2) No satisfactory approach to an equivalent of human lung cancer has been produced in animals after exposure to .

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concentrated doses of tobacco smoke produced by smoking machines. In spite of the fallacies of this particular experimental approach, then, there are still other reasons for denying any real analogy to the situation of smoking in the human, as follows:

(a) A certain English investigator exposed 160 mice for 18 months to cigarette smoke. That is for about half of their life span. The smoking mice actually lived longer than the nonsmoking mice.

(b) Another British investigator, by name Campbell, observed an increase in lung-tumor rate in mice from 8 percent to 80 percent when they were subjected to prolonged inhalation of dust from roads with a 2 percent content of tar.

* * *

I would finally state then that the total evidence I have tried to review fails to establish any sound basis on which a causative influence can be assigned to cigarette smoking in the production of cancer of the lung.
(Macdonald - H.R. 1957)

Dr. Clarence Cook Little who was Director Emeritus of Jackson Laboratory in Bar Harbor, Maine, a former president of two major U.S. universities, and a former Managing Director of the American Society for the Control of Cancer, now the American Cancer Society, as well as Chairman of the Scientific Advisory Board of the Tobacco Industry Research Committee and Scientific Director of the Tobacco Industry Research Committee (as the Council for Tobacco Research - U.S.A., Inc.

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was then known) also testified at the hearings held before the U.S. Congress in 1957. He also questioned the assertion that a causal relationship could be established by a statistical association without experimental confirmation.

> Inconsistencies evident concerning the claimed cause and effect relationship: Nonsmokers may and do develop lung cancer; the great majority of heavy smokers do not.
>
> * * *
>
> In other words, lung cancer is a relatively rare disease, and there is no necessarily simple cause and effect relationship with smoking habits. If there was, you would get, instead of perhaps 1 out of 20, 1 out of 40, 1 out of 50 heavy smokers developing it, as is often the case or perhaps 1 out of 10 where it is at its very worst, then you would find a very much higher correlation than that.
>
> It is not a simple single cause-and-effect proposition. The point is that it is not a perfect correlation. It is not a thing on which you can rely. It is a serious problem as to what causes lung cancer, but it still remains true that it is not a simple cause-and-effect relationship.

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* * *

> To establish a cause-and-effect relationship on statistical association without experimental evidence is not safe. It cannot be done. You may get an indication of something to look for, but to say that the case is finished, the evidence is all in, and that you can satisfy experimental scientists, all of them; that is not possible, because too many of us have seen too many statistical relationships which have not meant the "cause and effect" relationship.
> (Little - H.R. 1957)

In addition, Dr. Harry S.N. Greene, Chairman of the Department of Pathology, Yale University, New Haven, Connecticut, and a prominent cancer researcher also testified that the statistical associations did not establish that cigarette smoke was carcinogenic. He was especially skeptical about the applicability to the production of lung tumors in humans or even in mice of experiments which reported the production of skin cancers in mice.

> There is also considerable evidence that the constitutional makeup of the individual is very much concerned in the production of cancers in areas of irritation.

* * *

> Several comments are required with respect to the published statistics. Two points have been brought out in these studies that strongly suggest a conclusion contrary to that drawn by the investigators.

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First, the incidence of lung cancer has been found to be greater in cities than in the country and, second, the incidence is much greater in males than in females.

* * *

It should be noted also that the skin of the mouse rather than the lung of man was the object of study in these experiments. There is no surety that a substance capable of inducing cancer in mouse skin would also induce cancer in mouse lung - to say nothing of human lung. As a matter of fact, in our hands, the same tar failed to produce cancer in transplants of embryonic mouse lung, a material known to be highly susceptible to cancer-inducing substances.

* * *

Well, my feeling in this business is that there isn't anything in tobacco that is carcinogenic, that is going to do the individual any harm and, therefore, it is difficult for me to see how a filter could take out something that doesn't exist. (Greene - H.R. 1957)

The same year, 1957, Dr. Greene extensively discussed the question of cigarette smoking and lung cancer in the Introduction to a newly released book entitled, "Science Looks at Smoking" by Eric Northrup. Dr. Greene, as he had done before the United States Congress, expressed significant doubts that a cause and effect relationship between tobacco and lung cancer had been as yet proved. According to Dr. Greene, "The case against tobacco is derived mostly from statistical associations and some experimental work with animals." (Northrup 1957)

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He noted specifically that a coincident increase or decrease in frequencies does not necessarily mean that one happening is the cause of the other.

> Nearly everyone is familiar with the statistical studies purporting to establish a causal relationship between cigarette smoking and lung cancer. These studies have been the subject of a barrage of propaganda both in the press and over the radio, and the controversy has provided the entertainment world with much free talent. The arguments go on endlessly, for, like the question of how many angels can sit comfortably on the head of a pin, there are no pertinent data on which to base a definite answer. . . .
>
> The mere fact of a coincident increase or decrease in the frequency of given happenings does not necessarily mean that one is causally related to the other. (Northrup 1957)

The view that causation had not been demonstrated, which Dr. Greene expressed, also was forwarded by one of the world's leading statisticians and geneticists, Sir Ronald A. Fisher, of the U.K., in letters to the editor of the British Medical Journal. (Fisher 1957) It was Dr. Fisher's belief that the relationship of lung cancer to cigarette smoking could just as well be explained by a common genetic factor influencing both,

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as by causation. In 1959, Dr. Fisher's writings on the subject were collected and published in pamphlet form. (Fisher 1959)

Another prominent British scientist, Dr. T.W. Lees, also published a pamphlet in 1959 which contained a scholarly examination of the smoking-lung cancer controversy, noting the fact that while science generally regarded all cancer as being connected with the inevitable process of degeneration, it was lung cancer alone for which a "simple dominating external cause," was believed to be responsible.

> This conclusion [of the Medical Research Council, London], which in effect affirms that smoking is the major cause of lung cancer, is unqualified. In other common forms of cancer no specific cause is known. If there is an association between some factor and a form of cancer it is only a partial one. Nearly all other theories of cancer assume that the cancer is bound up with degeneration and dying - with living itself. Indeed why else has the cancer problem defied three generations of intensive study?
>
> It is difficult to believe that one form of cancer should have a simple dominating external cause.

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* * *

A simple explanation, at least as plausible as smoking and at least part of a general theory, for the increase in lung cancer is that the type of men who would have died forty years ago from pulmonary tubercle in their thirties did not die of this disease twenty years ago and now survive with attenuated or healed tuberculosis to die of lung cancer in their fifties.

* * *

We have shown, we hope conclusively, that there is no evidence, not even prima facie evidence, that smoking causes lung cancer.

We are not saying that smoking may not be a factor in cancer: no one can say that until the cause of cancer is known. All we say is that the onus of proof rests on those who assert that a clinically and scientifically improbable theory of cancer causation must be true: and so far no evidence has been produced to support that assertion.
(Lees 1959)

In the mid-1950s, the governments of Sweden and The Netherlands were also investigating the possible health risks of cigarette smoking, but had taken no firm position on the question of cancer causation. They both chose to concentrate their public health efforts on seeking to discourage smoking by young people. Thus, as reported in the Journal of the American Medical Association:

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SWEDEN

Lung Cancer and Government Control of Tobacco.

Tobacco is controlled in Sweden by a government-created monopoly. The Prime Minister was recently asked whether the government was ready to cooperate in an educational campaign concerning the injurious effects of nicotine; whether it would support a scientific investigation of the health risks of tobacco in general and cigarettes in particular; whether the monopoly's advertisements in favor of cigarettes were in the interest of the community and, if not, whether the government would supervise the advertising methods used; and, finally, whether the government would consider any measures calculated to keep cigarettes away from school children and other minors. (J.A.M.A. 1956)

In a press notice dated March 8, 1957, the Dutch Ministry of Social Affairs and Public Health reported:

> At the request of the Director-General of Public Health the President of the National Health Council set up a commission some time ago to inform him on the subject whether there is a possible connection between smoking--particularly the smoking of cigarettes--and lung cancer. This commission issued their report a short time ago. In said report it is stated that the commission have come to the conviction, based on statistical grounds, that there is a connection between the two. The question whether there is a causal connection and if so, how far, can naturally not be answered by statistics, but the other possible factors, which were likewise studied in extenso, all

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> proved to be less probable in this respect than smoking. Basing his opinion on this and other considerations the Minister of Social Affairs and Public Health opines that steps should be taken to restrain young people from smoking heavily and at an early age. (H.R. 1957, p. 601)

The British Ministry of Health (Parliamentary Report 1957) and the National Cancer Institute of Canada (NCI Canada 1958) also were examining the cigarette-cancer causation question during this period. A subcommittee of the latter organization's Advisory Committee on Records and Statistics, in its review, found smoking to be a statistical risk factor for lung cancer, but concluded that the causal hypothesis was not scientifically established.

> From the practical standpoint, further findings of a possible cause-and-effect relationship between lung cancer and cigarette smoking can be expected to come only from: (a) continuing epidemiological studies of the kind already reported and (b) further studies relating to the detection, isolation and biological assay of substances in tobacco smoke that may be suspect.
>
> In our opinion the most important fact arising from this review is the following: While it has not been established that cigarette smoking is a cause of lung cancer, statistical studies show that cigarette smokers have a greater risk of dying of lung cancer than have non-smokers and the risk increases with the amount smoked. (NCI Canada 1958)

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On November 28, 1959, Surgeon General Burney published an article in the Journal of the American Medical Association which contained the following conclusions regarding cigarette smoking and lung cancer:

> 1. The weight of evidence at present implicates smoking as the principal etiological factor in the increased incidence of lung cancer. 2. Cigarette smoking particularly is associated with an increased chance of developing lung cancer. 3. Stopping cigarette smoking even after long exposure is beneficial. 4. No method of treating tobacco or filtering the smoke has been demonstrated to be effective in materially reducing or eliminating the hazard of lung cancer. 5. The nonsmoker has a lower incidence of lung cancer than the smoker in all controlled studies, whether analyzed in terms of rural areas, urban regions, industrial occupations, or sex. 6. Persons who have never smoked at all (cigarettes, cigars, or pipes) have the best chance of escaping lung cancer. 7. Unless the use of tobacco can be made safe, the individual person's risk of lung cancer can best be reduced by the elimination of smoking.
> (Burney 1959, emphasis supplied.)

Moreover, the United States medical community remained divided on the issue, as seen from the following editorial statement in the Journal of the American Medical Association which concluded that neither the authorities who disagree with

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the Surgeon General nor those who agree, have sufficient evidence to warrant an "authoritative position."

> A number of authorities who have examined the same evidence cited by Dr. Burney do not agree with his conclusions. Although the studies reveal a relationship between cigarette smoking and cancer that seems more than coincidental, they do not explain why, even when smoking patterns are the same, case rates are higher among men than among women and among urban than among rural populations. Neither the proponents nor the opponents of the smoking theory have sufficient evidence to warrant the assumption of an all-or-none authoritative position. Until definitive studies are forthcoming, the physician can fulfill his responsibility by watching the situation closely, keeping courant [sic] of the facts, and advising his patients on the basis of his appraisal of those facts. The Public Health Service can best meet its obligations by collecting and disseminating data from all sources and making known to the health and medical professions its own evaluations of such data. (Talbott 1959)

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Mirroring the AMA's observation that neither proponents nor opponents of the smoking theory could carry the day, the appellate court in Lartigue (see p. 11, above) wrote:

> The plaintiff contends that the jury's verdict was contrary to the manifest weight of the evidence. The record consists of twenty volumes, not to speak of exhibits, most of it devoted to medical opinion. The jury had the benefit of chemical studies, epidemiological studies, reports of animal experiments, pathological evidence, reports of clinical observations, and the testimony of renowned doctors. The plaintiff made a convincing case, in general, for the causal connection between tobacco and cancer and, in particular, for the causal connection between Lartigue's smoking and his cancer. The defendants made a convincing case for the lack of any causal connection. The district judge, in the course of the hearing on the plaintiff's motion for a new trial, expressed the view:
>
> > I regret now I did not propound the interrogatory with respect to the connection between the smoking and his lung cancer because I'm satisfied the jury never got beyond that question and I know - I'm sure at least that they simply decided the

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> plaintiff had failed to prove the causal connection between his smoking and his lung cancer but that is water under the bridge now.
>
> We consider it unnecessary in this opinion to summarize the evidence. We find substantial evidence in the record to support the verdict.
> (Lartigue v. R.J. Reynolds 1963)

Dr. David T. Carr of M.D. Anderson Cancer Center, Houston, Texas, U.S.A., recently wrote that at the close of the 1950's, "many experts continued to doubt the significance" of epidemiological data which was claimed to causally relate cigarette smoking to lung cancer. (Carr 1989)

According to Dr. Matti Rimpela, it was not until the 1958-60 period that the Finnish medical profession "became conscious of the significance" of the claimed relationship between smoking and lung cancer. (Rimpela 1977)

4.3 The Advisory Committee To The United States Surgeon General

In March 1962, the Royal College of Physicians of London published its Report on Smoking and Health. It was concluded that "cigarette smoking is an important cause of lung cancer"; however, the report also concluded there was only a "strong association" between smoking and the incidence of chronic

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bronchitis which did "not necessarily mean that cigarette smoking is the chief cause or only cause of the disease." (Royal College of Physicians 1962) The report further noted that while various investigators had found an association between smoking and cancer of the mouth, larynx and oesophagus, "these forms of cancer are also associated with a high alcohol intake, which is also correlated with smoking so that it is difficult to interpret the evidence." (Royal College of Physicians 1962)

On June 7, 1962, the then Surgeon General of the United States, Dr. Luther L. Terry, announced that he was establishing an expert advisory committee to undertake a comprehensive review of all data on smoking and health. The names of more than 150 scientists were considered and, in the fall of 1962, a ten-person Surgeon General's Advisory Committee on Smoking and Health was established. The Advisory Committee and its staff examined much of the literature that had been published and, on January 11, 1964, released a Report to the Surgeon General. The Advisory Committee stated:

> It is recognized that no simple cause-and-effect relationship is likely to exist between a complex product like tobacco smoke and a specific disease in the variable human organism. It is also recognized that often the coexistence of several factors is required for the occurrence of a disease, and that one of the factors may play a determinant role; that is, without it, the

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other factors (such as genetic susceptibility) seldom lead to the occurrence of the disease.
(The 1964 Terry Report)

In the Forward to the Report, Dr. Terry stated:

> Since the turn of the century, scientists have become increasingly interested in the effects of tobacco on health. Only within the past few decades, however, has a broad experimental and clinical approach to the subject been manifest; within this period the most extensive and definitive studies have been undertaken since 1950.
>
> Few medical questions have stirred such public interest or created more scientific debate than the tobacco-health related controversy. The interrelationships of smoking and health undoubtedly are complex. The subject does not lend itself to easy answers. Nevertheless, it has been increasingly apparent that answers must be found.
> (The 1964 Terry Report)

Relying predominantly on statistical studies which had been conducted to date (and without conducting any research of its own), the Advisory Committee reached the following conclusions regarding lung cancer, chronic bronchitis and emphysema and laryngeal cancer:

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Cigarette smoking is causally related to lung cancer in men; the magnitude of the effect of cigarette smoking far outweighs all other factors. The data for women, though less extensive, point in the same direction.

The risk of developing lung cancer increases with duration of smoking and the number of cigarettes smoked per day, and is diminished by discontinuing smoking. In comparison with non-smokers, average male smokers of cigarettes have approximately a 9- to 10-fold risk of developing lung cancer and heavy smokers at least a 20-fold risk.

The risk of developing cancer of the lung for the combined group of pipe smokers, cigar smokers, and pipe and cigar smokers is greater than for non-smokers, but much less than for cigarette smokers.

Cigarette smoking is much more important than occupational exposures in the causation of lung cancer in the general population.

* * *

Cigarette smoking is the most important of the causes of chronic bronchitis in the United States, and increases the risk of dying from chronic bronchitis and emphysema. A relationship exists between cigarette smoking and emphysema but it has not been established that the relationship is causal.

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* * *

> Cigarette smoking is a significant factor in the causation of laryngeal cancer in the male.

The 1964 Terry Report did not find a causal relationship between cigarette smoking and cardiovascular disease.

The Cancer Bulletin, in giving a contemporaneous summary of the 1964 Terry Report noted that, "the relationship between smoking and lung cancer has been a hotly debated issue of the past decade." (Cancer Bulletin 1964)

As noted by Dr. R.H. Rigdon (see Exhibit B:8), the 1964 Terry Report did not reference many articles in which the authors expressed views in conflict with the causation hypothesis. An example of the omissions is a report by the noted British experimental pathologist, R.D. Passey, who found that neither the amount smoked nor the age of smoking onset affect the age when lung cancer develops.

> It is now accepted that smoking increases the risk of lung cancer, and that the heavier the smoking the greater the risk. But nowhere has it been claimed that the heavy smoker is stricken with cancer earlier than the light smoker. If lung cancer in smokers is a result of direct carcinogenic action, one would certainly expect this to happen; for experiment has shown beyond question that a potent carcinogen induces tumors early.

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I examined the smoking histories of 499 men with lung cancer (4 were non-smokers) and grouped the cases according to the number of cigarettes smoked (Doll and Hill 1952).

Table I shows that the amount smoked made no appreciable difference to the mean age at which the patient first reported to the clinic. The light smoker is afflicted with lung cancer at the same age as the heavy smoker. This is a surprising observation. The mean age at which smoking was started was seventeen; the average amount smoked daily was twenty-three cigarettes; and the mean age at which the patient presented at the clinic was fifty-seven years. On the average, death occurred some months later. The mean smoking period was some forty years.

It occurred to me that the youngest of these patients with lung cancer might have smoked particularly heavily, and that the eldest had survived because they were specially moderate smokers. But, put to the test (table II), this obviously is not so. The amount smoked daily by old and young is not dissimilar. Yet the oldest patient had smoked for some fifty years longer than the youngest - which represents well over a quarter of a million more cigarettes. These figures suggest that there is no relation between the amount smoked daily and the age of onset of lung cancer.

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> Nowadays, boys and girls begin to smoke much earlier and are confirmed smokers long before they have left school. But my figures (table III) show clearly that the disease developed at approximately the same age in those who began to smoke earliest (between the ages of six and ten) and in those who started to smoke much later (table IV). Those who started early smoked for some fifty-one years, whereas the late starters smoked for only thirty-one years or so; yet there was no great difference between the daily amounts which patients in each group said they smoked. Each member of the group which began early must have smoked over a hundred-and-fifty thousand cigarettes more than the late starters. These figures offer the clearest evidence that the age when lung cancer develops is determined by neither the amount smoked nor the age at which smoking began. If this is true, tobacco smoke did not act as a carcinogen. It is apparently not the number of cigarettes smoked but something related to the age of the individual which determines when he dies from lung cancer.
> (Passey 1962)

According to Dr. Lester Breslow, who was very actively involved in the Advisory Committee's activities, the 1964 Terry Report was more of an effort to alter policy towards cigarette smoking than a scientific investigation. He observed that the report was a "public policy venture" designed to campaign against cigarette smoking, rather than a "scientific venture" which sought to further investigate

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the relationship between smoking and lung cancer. In his words:

> By the early 1960s, we felt that the time had come to act. So we looked upon the Surgeon General's report, not so much as a scientific venture, although it was that--it was sort of a summary of the scientific work by a prestigious neutral body that could not be attacked because they had personally become involved with the studies--it was looked upon, not so much as a scientific venture, but as a public policy venture. That would make possible, we felt--I felt and I think others shared this view--the development of public policy in the country. So that was the feeling that I had toward it when it was being developed in '63-'64 and was published. And then we found that it could be used for that purpose. So from that point on, I was no longer interested in the investigative aspect of cigarette smoking and lung cancer, although increasingly interested in the relationship between cigarette smoking and other diseases. That became a matter of scientific investigation. But with regard to cigarette smoking, now the time had arrived to begin a public campaign against cigarette smoking.
> (Breslow 1975; Shimkin 1979)

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The political objectives sought by the publication of the 1964 Terry Report were successfully achieved in the United States and in the rest of the world as well.

5. THE ERA FOLLOWING THE REPORT TO THE SURGEON GENERAL

5.1 Legislative Restrictions In The United States Resulting From The Controversy

Shortly after the 1964 Terry Report was issued, the United States Federal Trade Commission announced a proposed rule which would require U.S. cigarette manufacturers to include warnings on cigarette packages and advertisements that cigarette smoking "is a health hazard" or "is dangerous to health," along with certain additional information. The FTC's proposal resulted in hearings on the subject before the Interstate and Foreign Commerce Committee of the U.S. House of Representatives in June and July of that year. In November 1964, a new Congress was elected and the following year extensive cigarette labeling and advertising hearings were held in both the United States Senate and the House of Representatives. The statements of over three dozen distinguished physicians and scientists were delivered or submitted at the 1964-65 hearings to the effect that it had not been scientifically established that cigarette smoking was a cause of

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human disease.* A representative selection from among those statements, detailing the scientific reasons for their conclusions, is attached as Exhibit B. The following were among the main themes of that testimony:

1. Research on differences in personality types between smokers and non-smokers supports the hypothesis that the statistical association between smoking and lung cancer may reflect an underlying genetic structure which accounts for both lung cancer and

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* U.S. Congress, House of Representatives, Committee on Interstate and Foreign Commerce, Cigarette Labeling and Advertising: Hearings 88th Cong., 2nd Sess., 23-25; 29 June and 2 July 1964. (Hereinafter cited as "H.R. 1964".)

U.S. Congress, House of Representatives, Committee on Interstate and Foreign Commerce, Cigarette Labeling and Advertising--1965: Hearings, 89th Cong., 1st sess., 6-9; 13-15 April and 4 May 1965. (Hereinafter cited as "H.R. 1965".)

U.S. Congress, Senate, Committee on Commerce, Cigarette Labeling and Advertising: Hearings, 89th Cong., 1st sess., 22-25; 29-30 March and 1-2 April 1965. (Hereinafter cited as "S. 1965".)

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the decision to smoke. This is supported by the fact that smokers and non-smokers differ in many other ways as well.

2. Statistical associations can provide hypotheses for further study but cannot, by themselves, be a sufficient basis for a conclusion of causality.

3. The peak incidence of lung cancer is at about 60 years of age. This is true for non-smokers as well as for smokers and in smokers it is maintained irrespective of the amount smoked or when smoking commenced.

4. Lung cancer rates vary by constitutional factors such as age, sex and race.

5. Cancers rarely occur in the trachea or in both lungs. The trachea is exposed to a great concentration of smoke and contains tissue of the same type as is found in the lung. This finding is inconsistent with the hypothesis that cigarette smoke (which passes through the trachea and into both lungs) is the causative agent.

6. Lung cancer does not occur in all persons who smoke and is found in many who do not.

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7. Efforts to corroborate the statistical association through animal experiments using inhalation of whole smoke have been negative.

8. Science does not know the mechanism which produces a cancer from previously normal tissue.

9. The apparent rise in lung cancer since the 1930s may be an artifact of improved diagnosis, changes in classification methods and the inaccuracy of death certificates.

10. The rate of increase of lung cancer declined during periods when the rate of smoking increased.

Dr. L. Henry Garland, whose testimony is quoted in Exhibit B, also noted to Congress that while it had been taught in medicine that most lung cancers arose in the main bronchi or the lobar bronchi, first or second division (where the concentrations of cigarette smoke are supposed to be greatest in the lungs), his research had found the majority of lung cancers occurred in the peripheral portions of the lung. (Garland-H.R. 1964)

Of course, many statements were submitted in the hearings which related cigarette smoking to

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human disease, including those of representatives of the public health establishment and voluntary health organizations. In the summer of 1965 the United States Congress enacted Public Law 89-92 which required the following statement to be placed on cigarette packages, but not in advertisements: "Caution: Cigarette Smoking May Be Hazardous to Your Health." It should be noted that the Congress required a warning that cigarette smoking may be a health hazard, and not that it was a hazard.

Meanwhile, in Finland, the Tobacco Committee, which was selected in 1964, reached the conclusion amid their investigations that the introduction of a mandatory warning on tobacco products would not be recommended because it was suspected that a warning would numb the senses of consumers and might even have a negative educational impact. The following statement of the Tobacco Committee is a good example of its views at that time:

> When the tobacco users get used to continuously seeing the warning in connection with a product they use daily, it may lead to indifference also in respect of pertinent education activity. The use of such a warning could also be held ethically

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> questionable. It is hardly appropriate to attach a warning to a product, the manufacture and sales of which is permitted specifically for such use, against which the warning is given, and from which the state collects considerable earnings. If the intended warning would be considered necessary to introduce, then the only acceptable action would be to prohibit the import, manufacture and sales of tobacco products which the committee does not consider possible.
> (Committee Report 1966: B69 pp. 54-55)

During the legislative year 1969, further hearings were held in the United States Congress on the subject of cigarette labeling and advertising. As in previous years, a significant number of distinguished scientists and medical doctors testified that there continued to be a scientific controversy as to whether cigarette smoking caused disease in humans. Included were Dr. Kenneth J. Kingsbury, a surgeon at St. Mary's Hospital in London, England, specializing in vascular disease, who said, "although there appears to be a relatively weak association between smoking and some of the symptoms of vascular disease, its meaning is unknown," (Kingsbury - H.R. 1969) and Dr. Lucio Severi, Director, Institute of Pathological Anatomy and Histology, and Division of Cancer Research, Perugia University Medical School, Perugia, Italy who concluded that more research was needed into the relationship between cigarette smoking and lung cancer because there had still been no experimental

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U.S. Congress, House of Representatives, Committee on Interstate and Foreign Commerce, Cigarette Labeling and Advertising - 1969: Hearings, 91st Cong., 1st sess., 15-18; 21-25; 28-30 April and 1 May 1969. (Hereinafter "H.R. 1969".)

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corroboration of the claimed relationship. He cautioned that efforts to prevent the disease are likely to be ineffectual unless preceded by an understanding of the disease.

> The problem of lung cancer still remains to be solved. We know a great deal about lung cancer, but not so much as we need to know, especially as far as aetiological factors are concerned. In relation to these there are two fields for study of particular importance: (a) cigarette smoking, because experimental evidence of its suspected responsibility is lacking; (b) certain drugs -- the antibiotics and the anti-tuberculosis drugs -- which could be of significance in the increasing incidence of lung scar cancer.
>
> As far as man is concerned, what is not understood cannot be prevented. For this reason -- and on this point let there be no doubt -- there is little to expect from prophylaxis, and much to hope for from basic research. From this point of view much systematic, methodical, step-by-step research with animal models must be done.
> (Severi - H.R. 1969)

In a statement submitted to the House of Representatives at the 1969 hearings, Professor Cecile Leuchtenberger, a Ph.D. Biologist, and Professor Rudolf Leuchtenberger an M.D. Experimental Pathologist, co-chairmen of the Department of Cytochemistry at the Swiss Institute for Experimental Cancer Research, Lausanne, Switzerland,

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quoted from one of their recently published research reports in which they concluded that the problem of lung cancer would not be solved until there was a full exploration of the many factors besides cigarette smoke which have also been associated with the disease such as genetics, diet, air pollution, etc.

> Human lung cancer is one of the most serious public health problems today. Although epidemiological, clinical and histopathological studies carried out on non-smokers and cigarette smokers have been interpreted as implicating inhalation of cigarette smoke as one of most important causative factors in the occurrence of human bronchogenic carcinoma, the problem is by no means solved, but requires additional research. The direct proof of a causal relationship between cigarette smoking and lung cancer in man faces the same difficulties that are inherent in any situation in which a large and unknown number of potentially carcinogenic and cocarcinogenic influences need to be explored. It is necessary to determine and elucidate the possible role of other suspected endogenous and exogenous factors, such as genetic constitution, air pollution, radiation, hormones, preceding diseases, nutrition, host viruses, environment and living habits, as well as that of cigarette smoke. Experimental exploration of the possible biological effect of these factors, alone or in combination with others, on the human lung is also necessary because many other important questions remain unanswered today.
> (Leuchtenberger - H.R. 1969)

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The 1964 Terry Report had concluded that predominantly epidermoid and oval-cell (WHO Group I) lung cancers and not adenocarcinomas (WHO Group II) had a statistical association with smoking. (The 1964 Terry Report) However, at the 1969 hearings, Dr. Doris L. Herman, a University of Southern California pathologist, testified that her extensive studies had found only a small difference in the percentages of Group I and Group II cancers (Herman - H.R. 1969). Concluding that this finding -- which had been confirmed in the Terry Report -- did not support the theory that cigarette smoking had caused an increase in epidermoid tumors, she urged further research into host factors which might determine why some individuals developed lung cancer and others did not.

> The theory that cigarette smoking has caused a rise in incidence of epidermoid tumors of the lung (Group I) is not supported by our studies. Since other areas of the United States show the same distribution of types of tumors as Los Angeles, the Los Angeles data cannot be dismissed as merely an unusual geographical result. On the other hand, there are areas in the United States and abroad which show a distribution of types of tumors very different from that of Los Angeles. Therefore, much more work is necessary before we can understand any possible relationships between types of tumors and possible causes.

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> Future work should include research in relation to host factors. Immunological, hereditary and endocrine characteristics may be important in determining why individuals get lung cancer. Extensive further investigation in these and other areas is needed to establish the causes of lung cancer, and to determine whether or not cigarette smoking is one of them.

The 1969 hearings also contained the remarks of Dr. Rune Ernst Cederlöf, an associate professor at the Department of Environmental Hygiene, National Institute of Public Health, Stockholm, Sweden. His studies of identical twins with discordant smoking habits led him to the conclusion that the association between angina pectoris and smoking may be statistical and not causal.

> The actual applications of the twin approach to the problem of smoking and health, which I have now reviewed, have, according to my opinion, clearly indicated that the association between smoking and the symptom 'angina pectoris' may be merely statistical and not causal. They have also shown that at least part of the association between smoking and 'cough' may be due to confounding factors.
> (Cederlöf - H.R. 1969)

Notwithstanding the extensive testimony that a controversy existed, the U.S. Congress yielded to the intense pressure for restrictions on cigarette advertising and on April 1, 1970, passed Public Law 91-222 which prohibited cigarette advertisements

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on radio and television. The law also amended the required statement on cigarette packages to read "Warning: The Surgeon General Has Determined That Cigarette Smoking Is Dangerous to Your Health." While the previous warning that cigarette smoking "may be" a health hazard was an equivocal statement, the amended warning was attributed as a conclusion of the Surgeon General. Thus, as late as 1970, after many weeks of hearings extending over several years, the Congress again declined to reach the conclusion that cigarette smoking constituted a danger to consumers.

5.2 The Traces Of The Controversy In Finland

The tobacco and health controversy was, particularly in the beginning, an Anglo-Saxon phenomenon which had its main stage in the United States. The controversy also echoed relatively soon in Finland, certainly in part due to its visibility in the press (cf. for example Reader's Digest, above) which awakened members of Parliament in Finland to make motions as early as the end of the 1950s. Following motions made during the 1958, 1959 and 1960 parliamentary sessions, the Parliament expressed to the government petitionary motion (1964 Parl.session - Parl.motion - Petit. res. No. 96)

> ... that Government would take urgent action to introduce legislation whereby sales of tobacco to children under certain age would possibly be totally prohibited, and to effectively restrict tobacco advertising, and

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also for other systematic actions against the use of tobacco

The motion did not at first result in any actions of the government, but when 102 members of Parliament, following the publishing of the 1964 Terry Report, questioned government why it had not taken any action in accordance with the motion, the Council of State finally on August 6, 1964 appointed a committee (the Tobacco Committee) "to review health hazards associated with tobacco smoking and possibilities to reduce them as well as to propose actions...." The Tobacco Committee did not itself study or cause any studies on health risks associated with smoking, but as it stated:

> When beginning its work the committee noted unanimously that it was not purposeful for the committee to study itself or cause any time consuming or extensive scientific studies on the health hazards of smoking, but it decided to make use of the already existing and quite abundant literature in the field (Committee Report 1966: B 69 p. 7)

The information it gathered from various sources the Tobacco Committee summarized in its report submitted on March 31, 1966 as follows:

> 2. <u>The Health Effects of Smoking</u>
>
> Of the sources available to the committee none, with one exception, even attempts to establish that any use of tobacco would have

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Source: https://www.industrydocuments.ucsf.edu/docs/hghl0000

beneficial health effects or that smoking would have no detrimental health effects. The one publication referred to (Oppers and Hoeflake) notes that smoking prevents obesity and since the average life time of corpulent people is believed shorter than that of the reasonably fed, smoking could in this respect be regarded as beneficial. The general understanding appears, however, to be that smoking is detrimental to health. There appears, however, to be a dispute in many respects on how smoking is detrimental and on how big the health risk thereof is. Accordingly, the well-known American study "Smoking and Health" (the Terry Report) finds it established almost with certainty, as do also numerous other studies, that smoking causes lung cancer. Instead, it does not find it established that the excess mortality of cigarette smokers in cardiovascular disease would with certainty be a consequence of smoking. On the other hand, the German study of Pochen, Mittman and Kneller which is often referred to in attempts to question the relation between cigarette smoking and lung cancer, does not find that cigarette smoking causes lung cancer. On balance it does, however, establish that abundant cigarette smoking shortens life by causing cardio-vascular disease. Whereas one Finnish report (Konttinen) states that the only disease which with certainty has been possible to establish to depend on smoking, is the so-called Burger's disease, the above mentioned "Smoking and Health" study does not conclude that this causal relationship is established with certainty.

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Based on the available literature it appears in any event certain that the general mortality among cigarette smokers is higher than among non-smokers or among cigar or pipe smokers. That this above average mortality with certainty would result from smoking does not appear to be possible to establish demonstrably, although such a causal relationship is highly probable."
(Committee Report 1966: B 69 pp. 8-9)

As the final outcome of its work the Tobacco Committee proposed eight actions, namely:

1. The research on the use of tobacco should be considerably more effective;
2. Information on the results of studies on the use of tobacco and health risks of smoking shall on a continuous basis be published through appropriate educational work;
3. A special advisory body shall be established to plan and direct the educational activities;
4. The state budget should reserve 1 per mille of the tobacco tax revenues to finance research and education;
5. A sufficiently high tobacco excise tax should be directed so that it above all would reduce the use of tobacco products detrimental to health;
6. A special supervisory body should be established to control tobacco advertising;

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7. The advisory body should periodically publish information on results from studies of additives and smoke analyses on tobacco products and cigarette papers; and

8. Generally more prohibitions should be implemented which would prevent smoking in certain meeting rooms, transport systems, etc.

Unlike in the United States, the Tobacco Committee did not recommend the use of an American type warning, for reasons stated above.

The first of the propositions of the Committee came through in 1969, when the Ministry of Trade and Industry and the Tobacco Manufacturers' Association agreed on certain restrictions on advertising and the ministry appointed a supervisory body to control the adherence to the agreement and good tobacco advertising practices otherwise, particularly in relation to young people.

From the beginning of the following year (1970) the Council of State appointed a standing advisory tobacco committee, to which the responsibility of the planning and direction of activities to reduce smoking was centralized.

Other measures to be mentioned are the prohibition of television advertising from the beginning of 1971 and the decisions of some municipalities to refuse tobacco advertising on advertising sites owned by them. The Medical Board guidelines for increasing the efficiency of health education in medical

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centers (DNo. 9721/505/70) mentions the reduction of smoking as one of three most important parts of health education.

The next step was the appointment by the Ministry of Health and Social Affairs on July 5, 1972 of a commission (the Tobacco Commission - called "commission" instead of "committee" to distinguish it from the 1964 committee, translator's note) which was commissioned to draft proposed regulations for the administration of the tobacco politics (Committee Report 1973:42). The Tobacco Commission was quite discordant and could not come to any conclusion whether tobacco advertising should be prohibited or not. Its proposals did, however, form the body of the later Tobacco Act Bill which resulted in the Tobacco Act that entered into force on March 1, 1977.

Finland, which started off in the tobacco and health issue with traditionally slow pace, rose with the Tobacco Act like a rocket to the front in anti-smoking activities, not so much as a result of any domestic controversy, but rather as a result of importing to Finland the official stance of foreign and particularly American controversies. To understand our own development, knowledge of the international and in particular the U.S. controversy is necessary.

5.3 Questions Continue In The 1970s

In the 1970s, many eminent scientists from Europe and the United States published articles which questioned the cigarette smoking-disease causation hypothesis. For example, Cole, et al. of the Medical Research Council of the Pneumoconiosis Research Unit in Penarth, Wales, in 1974 reported

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the results of a joint ten-year prospective study of a Danish and an English town. (Cole 1974) In the Danish town, the researchers found that nonsmokers had a higher death rate than those who smoked cigarettes, pipes and cigarettes plus other forms of tobacco. In the English town, they found that the "heavier" smokers had lower death rates than the "lighter" smokers.

During this period, Dr. Richard Doll continued to report his study of British doctors, but much of his data was inconsistent with the smoking-causation hypothesis. For example, there was no significant increase or decrease in overall mortality among British doctors age 65-74 compared with the same age group in the general male population, even though the doctors were reported to have given up smoking at a far greater rate than the general population. And, doctors in the age group 75-84 even experienced an increase in overall mortality compared to the general male population. (Doll 1976) In commenting upon this study in the British Medical Journal, Professor Philip Burch, a medical physicist at the University of Leeds, U.K., stated:

> [T]he temporal trends in overall mortality show no consistent association with the trend of smoking habits. Of course it can be objected, with justice, that it is pointless to compare mortality in the self-selected group of doctors who chose to answer Doll and

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Source: https://www.industrydocuments.ucsf.edu/docs/hgnl0000

Hill's first questionnaire with mortality in the general male population, which differs in so many constitutional and environmental respects from the responding doctors. (Burch 1977)

Questions continued to be raised about the increase in lung cancer cases reported to have occurred this century. Scientists observed that much of the increase in lung cancer might well be apparent rather than real and due to increased diagnostic accuracy. The principal techniques for diagnosing lung cancer--namely, x-ray, bronchoscopy, and sputum cytology--became widely available after 1930. Indeed, there was not even a specific disease category for lung cancer in the International Classification of Diseases until 1939. In contrast to the tendency to underdiagnose lung cancer in the early part of this century, many studies indicated that lung cancer in the 1960s and 1970s was overdiagnosed. For example, in autopsy studies Rosenblatt determined that only 40% of deaths listed as lung cancer on death certificates could be confirmed as cancer of the lung on histological review. (Rosenblatt 1971a; 1971b; 1973) Professor Rudolph Hoppe of the Rhine Province Land Institute in Duesseldorf, Germany, reviewed 20,000 cases of clinically diagnosed lung cancer in Northern Germany and was able to confirm only 62% of the diagnoses among males and 44% among females. (Hoppe 1977)

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Accordingly, many scientists were of the view that the so-called "epidemic" of lung cancer did not represent a true increase but rather reflected more sophisticated techniques for diagnosing a disease that had been extant for many generations, together with a tendency to overdiagnose the disease in recent years. For example, the Swedish pathologist, Dr. T. Berge of the University of Lund, stated in commenting upon the true incidence of lung cancer:

> It is obvious that the frequency figures based on clinical methods are too low in earlier series, whereas in recent series the figures may be too high because of overdiagnosis. This may give a false impression of the real increase. (Berge 1975)

Indeed, Professor Oeser of the Clinic for Radiology and Nuclear Medicine in Berlin showed that after adjusting for the different age structures of the then current population, compared with the population at the turn of the century, the total incidence of all cancers in the populations of the USSR, the United States, Norway, the Federal Republic of Germany and Switzerland had not changed. According to Professor Oeser, the total number of cancer deaths in a given population is related to its age structure, not its environment. (Oeser 1974; 1976; 1977 and 1978)

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Moreover, Dr. O. Parkash of the Departments of Pathology and Surgery at Wilhelminen Hospital in Vienna found that the incidence of lung cancer in Vienna had remained constant since 1962 despite the fact that tobacco consumption had been steadily increasing. (Parkash 1977) And a study of the changing pattern of lung cancer in the U.K. reported a fall in the incidence of this disease in men. (Belcher 1975; B.M.J. 1976)

In the 1970s, Dr. Philip R.J. Burch of the U.K. published papers in which he concluded that the smoking and lung cancer mortality data in Britain were more consistent with the constitutional hypothesis first postulated by the eminent statistician and geneticist Sir Ronald Fisher in the 1950s, than with the smoking causation hypothesis. (Burch 1972a, 1972b; 1973a, 1973b, 1973c; 1974a, 1974b, 1974c, 1974d, 1974e, 1974f, 1974g; 1975; 1976) Analyses of mortality data has been complicated by changes in the classification of lung cancer which tend to exaggerate the incidence of that disease by adding some cancers arising elsewhere to those arising in the lung. (Cf. ICD-8, ICD-9)

At hearings held on February 3, 1972 before the Consumer Subcommittee of the United States Senate Commerce Committee*,

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U.S. Congress, Senate, Consumer Subcommittee of the Committee on Commerce, Public Health Cigarette Amendments of 1971: Hearings, 92nd Cong., 2nd sess., 1,3,10 February 1972, pp. 88-96; 140-149; 459-592; 725-776. (Hereinafter cited as "S. 1972".)

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Dr. Sheldon C. Sommers, the research director of the Council for Tobacco Research-USA, Inc., was asked to provide the Committee with a list of the scientific papers published in the previous ten years which he thought should have been considered in the preparation of the U.S. Public Health Service's reports issued between 1964 and 1971, but were not considered. In response to that request, Dr. Sommers furnished the Committee with a bibliography of some 1,790 articles and books published since 1959 which had not been referenced in any of the reports issued to date. It was Dr. Sommers' view that the scientific papers he listed "should have been considered in any objective review of the literature because they tend to reveal the complexity of these diseases [which had been associated with cigarette smoking]." (Sommers - S. 1972)

In 1967, as requested by Congress, the United States Public Health Service issued its report on the Health Consequences of Smoking, and thereafter it published a series of these documents. In an additional 1977 paper, a representative of the Public Health Service stated:

> Although epidemiological data has clearly established the existence of a correlation between smoking and cancer, a clear-cut causal relationship between cigarette smoking and cancer has not been demonstrated.
> (Van Lancker 1977)

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The previous year, at hearings held on February 19, 1976 before the Subcommittee on Health of the Labor and Public Welfare Committee of the United States Senate,* the following exchange took place between Senator Gary Hart of Colorado and Dr. Theodore Cooper, Assistant Secretary for Health, U.S. Department of Health, Education and Welfare, the regulatory agency which has responsibility for the U.S. Public Health Service:

Senator Hart: I would merely ask if cigarette smoking causes heart disease?

Dr. Cooper: No.

Senator Hart: It does not?

Dr. Cooper: No.

(Cooper - S. 1976)

5.4 The Controversy Continues Into The 1980s

In the United States Congress, throughout the 1970s and 1980s, various bills were proposed to further restrict sales, marketing and advertising of tobacco products in the United States. A number of hearings were held, with the

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* U.S. Congress, Senate, Subcommittee on Health of the Committee on Labor and Public Welfare, Cigarette Smoking and Disease, 1976: Hearings, 94th Cong., 2nd sess., 19 February; 24 March; 27 May 1976. (Hereinafter cited as "S. 1976".)

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most extensive sessions occurring in 1982 and 1983.* At those hearings, some 39 scientists from Europe and America presented testimony supporting their opinions that the question of tobacco use and human health remained an unresolved controversy. Twenty of the scientists testifying were physicians and all were respected researchers in their fields.

1. Reports such as those of the U.S. Public Health Service have selected favorable evidence to review and ignored the results of studies contrary to their conclusions.

U.S. Congress, House of Representatives, Subcommittee on Health and the Environment of the Committee on Energy and Commerce, Comprehensive Smoking Prevention Act: Hearings, 97th Cong., 2nd sess., 5; 11-12 March 1982. (Hereinafter cited as "H.R. 1982".)

U.S. Congress, House of Representatives, Subcommittee on Health and the Environment of the Committee on Energy and Commerce, Smoking Prevention Education Act: Hearings, 98th Cong., 1st sess., 9; 17 March 1983.

U.S. Congress, Senate, Committee on Commerce, Science and Transportation, Comprehensive Smoking Prevention Act of 1981: Hearings, 97th Cong., 2nd sess., 16 March; 10 May 1982. (Hereinafter cited as "S. 1982".)

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Source: https://www.industrydocuments.ucsf.edu/docs/hghl0000

2. There were basic flaws in the methods used in the major epidemiological surveys that cast doubts on the accuracy of the claimed correlations.

3. No scientifically valid experiments in which animals were exposed to smoke produced the heart and lung diseases in question. Indeed, some smoking animals lived longer than the nonsmoking animals.

4. Studies had continued to report other factors associated with lung cancer, heart disease, emphysema and perinatal problems.

5. More research is needed if the causes of these diseases are to be known.

A more detailed summary of the above points made by the 39 scientists who testified at the 1982-83 hearings follows:

a. Several scientists testified that conclusions drawn in the recent reports of the Public Health Service were not necessarily valid because the reports were selective reviews. (Brown - H.R. 1982; Furst - S. 1982; Aviado - H.R. 1983)

b. According to testimony, the authors of the Public Health Service's reports apparently selected and reviewed

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primarily evidence that supported their case. The committees were provided with examples of contrary evidence that had not been reviewed in the reports and that should have been taken into account. (Hickey - S. 1982)

c. The Public Health Service's reports, wrote one widely published biostatistician, "have the characteristics of briefs for the 'prosecution' only; the 'defense' has been largely omitted even though these reports should have been unbiased. (Hickey - S. 1982)

d. A number of epidemiologists, statisticians and other scientists challenged the validity of inferences drawn from epidemiologic surveys that have reported a correlation between smoking and disease and that form a major part of the case against smoking. (Burch 1982; Roberts - H.R. 1982; Eysenck, Jacobson, Sommers - H.R. 1983; Macdonald, Sachs, Seltzer, Sterling - S. 1982)

e. Epidemiological surveys can only point out a statistical association between factors, such as smoking and disease, but cannot determine whether the relationship is causal. (Sterling - S. 1982)

f. Smokers, ex-smokers and nonsmokers have been reported to have different behavioral patterns. Because they made their own decisions

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about smoking they constitute "self-selected" samples. Both these and other factors can bias an epidemiological study and cast doubt on its conclusions. (Jacobson - H.R. 1983)

g. Many factors other than smoking are believed to affect health, including general lifestyle, alcohol consumption, occupational and environmental exposures, genetics, aging and the immune processes. These were not considered adequately in the large-scale surveys. When these factors are examined, results may differ from the findings of the large-scale studies relied on by the Public Health Service's reports. (Macdonald - S. 1982; Roberts - H.R. 1982)

Many witnesses also concluded that there were methodological flaws in specific surveys cited in the Public Health Service's reports which made their correlations uncertain. For example, these scientists pointed out it is scientifically incorrect to project disease rates in surveyed populations of smokers to the population as a whole when the groups studied are not representative of the whole.

The American Cancer Society's "million-persons" study by Hammond in the 1950s and 1960s earned especial attention. A scientist who reexamined the data from this study -- on which the conclusions of the Public Health Service's reports have relied strongly -- testified that the nonsmoker and smoker populations:

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- Were not randomly selected.

- Contained proportionally more smokers than the U.S. population.

- Were not representative of the population in age distribution, education or race.

- Contracted disease at different rates than the U.S. population.

- Lived in only 25 states, which were predominately urban industrialized, with little rural representation.

- Were interviewed by inexperienced volunteers. (Sterling - S. 1982)

Some of the witnesses were critical, too, of other studies cited in the Public Health Service's reports. One witness, Eleanor J. Macdonald, Professor Emeritus of Epidemiology at the University of Texas, had spent her lifetime studying the epidemiology of cancer; her comment is typical:

> There is a concept widely accepted by public health schools that if many studies, in themselves not based on definable populations, all arrive at the same conclusion, then that conclusion must be valid. This concept

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disregards the fact that the same intrinsic error in method might produce the same result.
(Macdonald - S. 1982, emphasis supplied.)

Several of the scientists testified about studies that raise questions about the conclusions from surveys cited in the reports of the Public Health Service. They said many of these studies had not been reviewed in the reports. (Hutcheon - S. 1982; Rao, van den Berg - H.R. 1983)

Among the evidence cited:

- Studies in the U.S. indicate that, when other environmental and lifestyle factors are considered, smoking cannot explain the ethnic and geographic patterns of lung cancer mortality.

- A number of new studies suggest such factors as nutritional and economic status--not smoking--to be strongly correlated with perinatal problems. These confirm the findings of older studies questioned by supporters of the causal theory.

One scientifically accepted step in evaluating a statistical correlation is animal experimentation. Such work can present both positive and negative results. The negative result is as important to the advancement of knowledge as the positive.

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A number of researchers presented evidence on cigarette-smoke inhalation experiments which had been conducted with animals. (Buhler - H.R. 1982; H. Fisher, Furst - S. 1982; Aviado, E. Fisher, Hockett, Schrauzer - H.R. 1983) Several had been directly involved in animal experiments seeking to determine if smoking causes lung cancer or emphysema.

These were among their conclusions:

- No scientist had been able to produce lung cancer or emphysema in laboratory animals with whole fresh cigarette smoke.

- Some studies were scientifically unacceptable because the animals were "smoked" at a rate equivalent to man's smoking 600 cigarettes per day. Others were confounded by infection or inhalation by the animals of extraneous material, such as dust.

- In some experiments, the groups of smoking animals contracted fewer tumors or lived longer than the nonsmoking groups.

According to the testimony, reports of the U.S. Public Health Service have ignored or minimized the importance of negative animal results and have ignored published criticisms of the animal work relied upon in their conclusions.

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5.4.1. Evidence Regarding Lung Cancer Presented at the 1982-83 Hearings

There were many presentations to the Congressional committees, some for and some against the proposition that smoking has been proven to cause lung cancer.

The scientific testimony summarized above underscores the inconclusiveness of the epidemiological and animal experimental work cited by those who accept the causal theory. There was also testimony on lung cancer which dealt with contradictory evidence; with disease trends and diagnostic errors; with pathological findings and with physiological factors.

5.4.1.1 Contradictory Evidence

Many witnesses explained why they considered the hypothesis that cigarette smoking causes lung cancer to be unproven, including Doctors Buhler (H.R. 1982), Burch (Burch 1982), Eysenck (H.R. 1983), Hickey (S. 1982), Macdonald (S. 1982), Schrauzer (H.R. 1983), Sommers (H.R. 1983), Sterling (S. 1982), E. Fisher (H.R. 1983) and others. (Booker, Farris, Herrold - S. 1982; LaVia, Rothschild - H.R. 1983)

They cited results of research to support their conclusions. Among the considerations mentioned were:

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- Smoking is neither a sufficient nor a necessary cause of lung cancer. The vast majority of even heavy smokers do not get lung cancer while among those who do contract the disease more than 10 percent are nonsmokers.

- When smoker and nonsmoker lung cancer mortality ratios are compared there are large and significant differences among the populations of different countries--particularly between Caucasians and Asians; between population subgroups within countries--by race as well as by sex; and between urban and rural dwellers and persons in residential and industrialized suburbs.

- Some studies report that factors such as lifestyle and residential and workplace pollution are correlated with lung cancer.

- There is evidence that hereditary and genetic factors play an important role in lung cancer incidence.

5.4.1.2 Disease Trends and Diagnostic Errors.

A number of witnesses were critical of the claim that cigarette smoking has caused an "epidemic" of lung cancer. Here, too, the experts cited evidence from recent studies.

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These were among the points made:

- In the early part of the century lung cancer was underdiagnosed, while in recent years it has been overdiagnosed.

- Changes in the rates of increase of lung cancer diagnosis have occurred simultaneously in men and in women, although, generally, women took up smoking some 30 years later than men.

- Significant increases have occurred recently in the incidence of lung cancer among nonsmokers.

- Changes in the International Classification of Diseases since 1948 have brought together, for the first time in official mortality records, cancers that originated in the lung and some of those that had spread to the lung from another body site. Major internal cancers frequently metastasize to the lung. Hence combining some secondary with primary lung cancers has resulted in a continued recorded increase in lung cancer while hiding the true incidence of cancers originating elsewhere in the body.

- Combining primary and secondary lung cancer for reporting mortality has made it impossible accurately to establish a statistical relationship of primary lung cancer and any agent or factor, including cigarette smoking.

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- Persistent errors in diagnosis of lung cancer as recorded on death certificates continue to cast doubt on the validity of statistical correlations in epidemiological studies and of claimed mortality patterns and trends.

5.4.1.3 Pathological Findings

Pathological data in both humans and animals were discussed by eight scientists.

Dr. Katherine Herrold (S. 1982) gave special attention to the relevance of conclusions drawn from epidemiological surveys. Now retired from the U.S. Public Health Service, the pioneering physician was a member of the U.S. government team that in 1958 reported results of a survey of 300,000 U.S. veterans, one of the first, and largest, of the prospective studies now used to support the causal theory.

Dr. Herrold subsequently reviewed the clinical and pathological data of the lung cancer patients in the veterans study. She told a Congressional committee she found:

- No correlation between various lung cancer cell types and the amount of tobacco smoked.

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- No relationship between the age at death and the age at which smoking started, the number of years of smoking or the number of cigarettes smoked per day.

Dr. Herrold pointed out that these results were almost identical to the findings made some 10 years earlier by the late Dr. R.D. Passey, and those of Doll and Hill in their study of British doctors in the 1950s and 1960s.

Another witness, Dr. Victor B. Buhler (H.R. 1982), a pathologist, challenged the claim that cell changes reported in the lungs of smokers are "precancerous," an argument made frequently by proponents of the causal theory. Dr. Buhler, the past president of the College of American Pathologists, said such changes appear also in nonsmokers. He said his testimony was based on "examination of thousands of lungs in microscopic detail." Despite his long experience, he said, he could not confirm that significant cell changes in the lung occur more frequently in smokers than in nonsmokers.

Other research on pathological findings that was cited by the witnesses at the 1982-1983 Congressional hearings included:

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- Central European hospitals, which regularly conducted autopsies, found lung cancer as early as the 19th century, when cigarette smoking was practically unknown. The lung cancer incidence reported then was similar to that of today, although the disease was not officially diagnosed in 90 to 95 percent of the cases.

- Errors in the stated cause on death certificates range from 30 percent to 60 percent.

- Except at autopsy, it is not possible to determine whether lung cancer is primary or secondary, and only about 12 percent of deaths in the U.S. from all causes today are autopsied.

5.4.1.4 Physiological Factors

Drs. J.M. Farris (S. 1982) and H.T. Langston (H.R. 1983), two eminent surgeons told why, based on their own clinical observations, they do not accept the causal theory. Among the points made:

- Although both lungs of the cigarette smoker are exposed equally to smoke, lung cancer rarely occurs in both simultaneously. It is also rare for a subsequent lung cancer to appear after successful treatment of the first.

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- Lung cancer occurs most often in the parts of the lung least exposed to smoke.

- Cancer of the trachea is rare even though the trachea, or windpipe, is exposed to all smoke going into and out of the lungs. Anatomically, embryologically and physiologically, the trachea is identical to the rest of the bronchial airway.

- Cancer of the larynx and tongue is rare. Yet the mouth and voice box are exposed to at least the same smoke concentration as the lungs.

- Nonsmokers get a type of lung cancer identical to that in smokers.

- The rate of increase of the incidence of lung cancer has fallen--as predicted more than 20 years ago--regardless of smoking rates.

In summary, these experts were of the opinion that it was not possible to scientifically conclude that cigarette smoking causes lung cancer, because of flaws in the basic epidemiologic studies, the failure to reproduce lung cancer in animals with whole smoke and recent work that has reported other factors associated with the disease.

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Source: https://www.industrydocuments.ucsf.edu/docs/hghl0000

The scientific witnesses agreed that far more research was needed to find the cause or causes of lung cancer and the mechanisms of the disease. As an example, Dr. Hans J. Eysenck (H.R. 1983), Professor of Psychology at The University of London, England stated:

> [T]he causal theory of smoking as being responsible for lung cancer and coronary heart disease, while it has found many supporters, is far from being established, and has many gaps, anomalies and contrary findings to contend with; these are too frequently glossed over and dismissed as unimportant, when in reality they may be found to discredit the causal theory in whole or in part. . . .
>
> What is certain is that at the moment no final decision can be made about whether, or the degree to which cigarette smoking may cause lung cancer or coronary heart disease, how it interacts with other factors (stress, personality), or how we can best protect the health of our citizens in relation to these diseases.
>
> "In ignorance, abstain" warned the famous French Scientist, Claude Bernard; hasty action on the basis of partial knowledge is unlikely to be in the best interests of those most concerned, namely the prospective victims of lung cancer and coronary heart disease.

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5.4.2 Evidence Regarding Coronary Heart Disease Presented at the 1982-83 Hearings

Several scientists questioned evidence presented to the committees on the alleged causal relationship between smoking and coronary heart disease (CHD). Citing their own research or review of the literature, the scientists presented reasons why they could not support the causal theory. (Russek - H.R. 1982; Bick, Gibbons - S. 1982; Bing - H.R. 1983)

Among the reasons:

- The relationship between smoking and heart disease is neither strong nor consistent--among populations of different countries, among those within a country or between men and women. For instance, while a statistical correlation between smoking and CHD has been reported in the U.S. and some other countries, none has been found despite similar scrutiny in Finland, Holland, Yugoslavia, Italy, Greece or Japan.

- The substantial decline in heart disease mortality rates in the U.S. in recent years cannot be explained by smoking patterns.

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- While smoking has increased among Swiss women in the last quarter century, their rate of heart disease declined significantly in the same period.

- The U.S. government's ongoing heart study in Framingham, Massachusetts, showed no excess CHD in male smokers over 55 years of age, and no relationship in women of any age.

- Other recent studies have reported similar results and found that ex-smokers have less CHD than nonsmokers.

- Although some have claimed women who smoke and take oral contraceptives suffer more strokes and heart attacks, supporting evidence is limited, weak and controversial and the object of severe criticism from impartial experts. Several studies have come to the opposite conclusion.

- Some types of CHD, for instance angina pectoris, are not reported to be statistically correlated with smoking. And pipe and cigar smoking have not even been statistically linked with CHD.

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Source: https://www.industrydocuments.ucsf.edu/docs/hghl0000

- Other factors, including heredity, emotional stress and environmental exposures and diet, have been reported in recent studies to be related to the incidence of CHD. Studies with identical twins have suggested a strong genetic influence in CHD incidence.

- Perhaps most important of all, no mechanism has been established to explain how tobacco smoke might cause CHD.

The testimony of these witnesses may be summed up by the statement of Dr. Carl Seltzer of Harvard, who wrote, "The bill's proposed warning, 'Cigarette smoking is a major cause of heart disease,' is not scientifically valid." (Seltzer - S. 1982) His call for more research was echoed by most of the scientists who opposed the claims about heart disease at the 1982-1983 hearings.

5.4.3 Evidence Regarding Chronic Obstructive Pulmonary Disease Presented at the 1982-83 Hearings

Drs. Aviado and Hockett (H.R. 1983) also questioned the assertion that cigarette smoking has been shown to cause emphysema and chronic obstructive pulmonary disease (COPD). Among the observations made were:

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- Emphysema had not been produced in laboratory animals by long term exposure to cigarette smoke. Emphysema has been induced in animal models with other inhalants.

- Epidemiological studies suggest that a number of risk factors are associated with COPD, among them outdoor and indoor air pollution, alcohol consumption, previous infections, familial predisposition and genetic susceptibility. Discussion of these in the Public Health Service's reports has been minimal.

- The causes of COPD have not been established and will be found only through further research.

Many other scientists, with various views on causation, have published articles in respected journals during this decade which nevertheless support a view that cigarette smoking has not been shown to cause the diseases with which it is statistically associated. Thus, Dr. Sakari Tola of the Department of Epidemiology and Biometry Institute of Occupational Health in Helsinki, Finland, has written:

> When male cancer cases were considered according to cancer type, lung cancer mortality differed statistically

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significantly between different occupational groups. The highest Standard Mortality Ratios (SMR's) were 225 for mining and quarrying; 190 for construction work; 188 for unskilled work; 170 for food production; 153 for forestry work; 146 for chemical processing; 145 for sheet metal work, welding, plumbing, and construction metal work; 143 for the use and service of work machines and stationary engines; 136 for fitting-assembling and machine and motor mechanic work; 135 for construction carpentry; and 122 for unskilled construction work. The lowest SMR's were for public administration (SMR 45), technical work (SMR 56), and farming (SMR 69). A similar occupational distribution of lung cancer incidence has also been published recently.

Although smoking may explain many of the differences, it is improbable that all the differences, especially the largest ones, between occupational groups would be explained only by smoking, since smoking is relatively evenly distributed between different occupational groups. (Tola 1981)

The British journal, Nature, cautioned against the acceptance of causation from statistical associations when the causal mechanism is unknown, and urged epidemiologists to acknowledge "the possibility that their statistical association may be wrong."

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It is also now to be taken as a fact that people who smoke cigarettes are more likely than others to develop lung cancer. The habit of smoking cigarettes is thus in some sense a cause of lung cancer. The link is clear enough for individuals prudently not to smoke cigarettes and for governments to encourage abstention. Yet the habit of smoking is not a first cause of lung cancer. That distinction no doubt lies with a group of chemicals not yet conclusively demonstrated. The mechanism by which lung cancer develops is not known, with the result that there is even room for argument about the influence of unknown genetic factors in the development of the disease. Such difficulties do not of course vitiate the epidemiological approach to cancer. On the contrary, there is undoubtedly great benefit to be won, both in the recognition of specific hazards and in the wider understanding of the natural history of cancer. Prudent practitioners are, however, careful not to make too much of the associations they find between effects and their supposed causes....

Epidemiologists should acknowledge the possibility that their statistical association may be wrong. Self-doubt is not merely seemly but persuasive.
(Nature 1981)

This same concern regarding the establishment of causation of coronary heart disease from epidemiology and "risk

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factors," such as smoking, was expressed by Drs. McCormick and Skrabanek of the Department of Community Health, University of Dublin, Ireland:

> Epidemiology has been preoccupied with the identification of "risk factors" for common degenerative diseases, such as cancers and coronary heart disease (CHD), whose aetiology and pathophysiology are poorly understood and whose treatment is disappointing. For coronary heart disease, the identification of risk factors has led to the belief that modification of such factors could prevent or reduce its incidence. While epidemiological studies may lead to the formulation of important hypotheses about the causes of coronary heart disease, only experiment can prove causal relations. Introgenic harm to both individuals and populations may be caused by premature translation of hypotheses into action.
>
> * * *
>
> Thom's analysis of trends in mortality from heart disease in 26 countries, between 1950 and 1978, conflicts with any simple notion of a direct causal link between risk factors and coronary heart disease. The most striking feature of these trends is an almost uniform decline of mortality in women, which is accompanied by an increase in mortality in men in many countries. Changes in smoking habit during these years were in the opposite direction to that which would be expected:

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men smoked less while women smoked the same amount or more.
(McCormick 1988)

Dr. J.R. Belcher, of the London Chest and Middlesex Hospitals has followed lung cancer statistics for a number of years and has published several articles containing his findings. In one of his recent papers, Dr. Belcher makes the following observation about the possible role of air pollution:

> The significance of pollution of one sort or another is not confined to the Western World. In Taiwan the incidence of bronchial carcinoma rose almost parallel in the two sexes since 1954 despite the fact that 29% of the men smoked as opposed to 2.1% of the women. The incidence was very much higher in the urban areas and the number of petrol vehicles had risen tenfold during the previous 20 years. Similarly, in Japan, the incidence of the disease had risen rapidly and almost equally in both sexes although only 12% of the women smoked as against 75% of the men. Lastly, in Hong Kong where the incidence of bronchial carcinoma in women is only second to that of their Maori sisters who have the highest incidence in the world, it has been shown that there is a strong relationship between the occurrence of the disease and the practice of cooking on kerosene stoves. All these observations suggest that there are important factors

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other than the cigarette in the aetiology of bronchial carcinoma, and that the most likely one is pollution in one form or another.

* * *

Lastly, as long as 20 years ago it was suggested by Lees that lung cancer was passing through the country like a 'wave' with the mortality and morbidity diminishing rather in the same way as it had done with tuberculosis and with scarlet fever, measles, and more recently duodenal ulcer. Lees produced more data supporting this view in 1971. It is suggested, as it was in 1975, that the figures presented here are best accounted for by this idea, that the aetiology of bronchial carcinoma and the changes which are occurring in its incidence are not entirely due to the cigarette, and that it is thus important to investigate all other possible factors.
(Belcher 1987)

To date, the proponents of the cigarette-cancer causation theory have been unable to explain scientifically the mechanism by which lung cancer occurs. Even the U.S. Public Health Service in its 1982 report agreed that "major efforts should be devoted to the elucidation of the steps involved in the formulation of lung tumors." (U.S. PHS 1982)

6. THE CONTROVERSY REGARDING SMOKING AND CANCER OF THE LARYNX

Although laryngeal cancer has been said to be statistically associated with smoking, reported rates of larynx cancer have not increased

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substantially over the last several decades, in contrast to reported lung cancer rates. If smoking causes laryngeal cancer, and given that cigarette smoking became popular in the 1920s and 1930s, larynx cancer rates should have increased concomitantly in the 1940s, 1950s, 1960s and 1970s. To the contrary, larynx cancer rates have not done so, and lung and larynx cancer rates have demonstrated marked disparities. (Doll 1977; Doll 1985) The same anomalous failure of larynx cancer rates to rise over time has been noted in Australia and Great Britain. (Austin 1982) Laryngeal cancer rates in Bombay, India, have been among the highest in the world, but lung cancer rates there are rather low. Also, women of the Maori tribe in New Zealand have the highest female rate of lung cancer in the world, but their larynx cancer rate is almost zero. (Austin 1982)

In this vein, one of the most vehement critics of cigarette smoking has said:

> If I wanted to argue that cigarette smoking was not proved to be the cause of any type of cancer, I would point to the trends in cancer of the larynx in various countries. Although this cancer has been closely related to cigarette smoking in all case-control studies, the trends in incidence and mortality have sometimes been in the opposite direction to the trends for cancer of the lung.
> (Doll 1981)

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Indeed, the second Report on Smoking and Health of the Royal College of Physicians of London, which was issued in 1971, again concluded that a causal relationship existed between lung cancer, and some other ailments, and cigarette smoking, but as in the first report, found larynx cancer only to be associated with smoking ("since, however, in respect of cancer of the mouth and larynx there is also an association with heavy drinking, alcohol may also contribute to their causation."). (Royal College of Physicians 1971)

In England and Wales, one study has found that laryngeal cancer mortality has consistently gone down as smoking has gone up, and that the ratio of men to women who have laryngeal cancer has consistently remained about 4:1, despite the increase of smoking by women in recent decades. The authors conclude:

> [U]nlike cancer of the lung, there was no sign of a following trend [i.e. as smoking goes up, cancer rates go up] in either mortality rates or male:female ratio which would give sound epidemiological grounds for a causal relationship between cigarette smoking and laryngeal cancer.
> (Ramadan 1982)

The authors also note that "there is conflicting evidence regarding the role of tobacco smoke in the development of laryngeal cancer . . . ." (Ramadan 1982)

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A similar divergence in trends was noted in a report from Scotland. (Boyle 1980) Although the percentage of smokers in Scotland was high and an increasing amount of tobacco was being consumed, the authors did not find the higher death rates in smokers that would be predicted under the causal hypothesis. Nor could they account for this same divergence in an area of western Scotland where the quality of data was high. Even though the authors stated there is scientific evidence suggesting a causal relationship of smoking to laryngeal cancer, they were forced to recognize that their own data presented an "anomaly."

The causal hypothesis also is not supported by a study in Argentina examining the smoking habits of cancer patients in three cities. Ferrara found that smoking did not have a statistically significant relationship to laryngeal cancer. This finding was interpreted as "not indicating a dependency between the presence of the studied cancer and the smoking habit." He concluded that "we can therefore hypothetically assume that other factors, besides the significance of the smoking habit, must logically affect the etiology of these pathologies." (Ferrara 1970)

In addition, cancer of the larynx is not a very common cancer. In Finland, during the period 1976-1980 the average annual number of reported new larynx cancer cases among males was

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121, while the average annual number of all types of new cancer cases was some 6,799. (Hakulinen 1986) Thus, larynx cancer constituted but 1.8% of all cancers. In the United States during that same time period, laryngeal cancer represented a similar small percentage (2.2%) of all reported new cancer cases among white males. (Horm 1984)

The statistical risk for developing laryngeal cancer has been shown to vary greatly, depending on gender, race, ethnic differences, geographic, socioeconomic status, and various other factors:

> (1) There is a significant variation between males and females worldwide. Of the 9,200 cases reported in the U.S. in 1978, 8,100 were in men and 1,100 in women. Furthermore, between 1935 and 1970, the incidence of laryngeal cancer in women has shown only a very minimal increase in spite of the fact that lung cancer in women has quadrupled during that same period. (DeVita, et al. 1985) About 2.3% of all malignant tumors in males but only 0.4% of all malignant tumors in females are laryngeal cancers. For males, there are 8.5 cases of laryngeal cancer per 100,000, compared to 1.3 cases per 100,000 for females. (Thawley 1987)
>
> (2) There is a marked variation between whites and nonwhites. From 1935

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to 1970, cancer of the larynx in the U.S. increased by 33% in white males, but increased by 350% in nonwhite men. (DeVita 1985)

(3) There are considerable geographic differences in larynx cancer rates. In parts of India, laryngeal cancer accounts for 7% of all cancers. In Japan, laryngeal cancer constitutes only about 0.7% of all cancer deaths. The incidence of laryngeal cancer is nearly identical in four Scandinavian countries (0.2 per 100,000 in Sweden, Iceland and Norway; 0.3 per 100,000 in Finland). This should be compared to rates for cancer of the lung and bronchus (70.7 per 100,000 in Finland; 13.5, 13.8 and 13.9 per 100,000 for Iceland, Norway and Sweden, respectively). (Austin 1982)

(4) There are differences in the occurrence of laryngeal cancer between urban and rural areas. One study reported that the rate of laryngeal cancer was nearly twice as high in urban areas as in rural areas. (Blot 1978)

(5) As socioeconomic status goes down, laryngeal cancer rates go up. (Blot 1978)

(6) There are ethnic differences in laryngeal cancer rates. Larynx cancer rates are particularly high in areas in which there are large numbers of people of Irish descent.

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They are also high in areas in which large groups of people of Polish, southern European and British descent live.
(Blot 1978)

(7) Many authorities have observed that nutritional deficiencies are strongly associated with cancer of the larynx. For example, studies have shown an elevated risk being associated with deficiencies in vitamin A, vitamin C, iron, and magnesium.
(Meyer-Breiting 1988)

(8) In a similar vein, it has been shown that there is an association between poor oral hygiene and laryngeal carcinoma.
(Elwood 1984) A positive association between use of gargles and mouthwashes and laryngeal cancer also has been detected.
(Zagraniski, 1986)

In recent years, a number of investigators have suggested that the human papilloma virus may play a causative role in the development of cancer of the larynx. (Syrjanen 1989; Brandsma 1989; Kashima 1986; Syrjanen 1982)

A number of studies show that there is a greater statistical association between alcohol consumption and laryngeal cancer than between smoking and that disease. This suggests that the statistical association between smoking and larynx cancer could be due to the confounding effects of alcohol use. Even Doll and Peto, severe critics of smoking, have said:

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> To say that certain conditions are related to smoking does not necessarily imply that smoking caused (or prevented) them. The relationship may have been secondary in that smoking was associated with some other factor, such as alcohol consumption or a feature of the personality, that caused the disease.
> (Doll 1977)

Tuyns and Audiqier conducted a study in France of several cancers in French males who were young adults prior to World War II. (Tuyns 1976) Among their findings was that cancer of the larynx was elevated. During World War II, alcohol availability and consumption were drastically reduced, but tobacco was still readily available. Cancer of the larynx fell in those cohorts who were young adults during World War II, but continued its rise in cohorts who were young adults after the war, when alcohol was again more heavily consumed.

McMichael, reviewing death statistics in England and Australia, also emphasized the importance of alcohol as a risk factor for laryngeal cancer (McMichael 1978), and in 1982, Ramadan, et al., stated:

> While the traditional role of cigarette smoking as an etiological factor in the development of laryngeal cancer has been brought into question, an increased alcohol consumption has emerged as being clearly associated with an increased risk of laryngeal cancer.
> (Ramadan 1982)

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Several occupations have also been epidemiologically associated with laryngeal cancer. It has been associated with mining in a number of countries (Block 1988; Zelma 1987) including Finland. (Teppo 1980) Asbestos workers, brewers and bartenders, machinists, stevedores and dock workers, seamen, and meat cutters all have elevated rates of larynx cancer. (Doll 1981) Other occupational settings in which a higher than predicted incidence of laryngeal cancer has occurred are woodworking, nickel refining, metal handling and processing (including grinding), leather working, farming and textile processing. (Zagraniski 1986) Laryngeal cancer mortality also tended to be higher in U.S. counties where there were heavy concentrations of chemical and printing industries. (Blot 1978) Some studies have found an excess risk of laryngeal cancer in cement and concrete workers and masons who would be exposed to dusts in their occupations (Zagraniski 1986) and one study found an elevated risk for persons exposed to "any occupational dust." (Olsen 1984) In light of the possibility that carcinogenic dusts could become impacted in the larynx, one study has suggested further study of dusty occupations. (Zagraniski 1986)

The epidemiological evidence is too disparate to support the claim that smoking causes cancer of the larynx. Similarly, animal data does not support a causal hypothesis. Although some scientists claim larynx cancer can be produced in hamsters, the evidence is problematic. The hamster larynx is

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extraordinarily narrow in comparison with other animal species and humans. Tar deposition data show hundreds of times the amount of tar deposits in hamster larynxes as compared with deposits in the hamster lungs when surface area is taken into account. (Bernfeld 1979) Thus, the claimed successful experiments were basically internal skin paintings.

Moreover, the hamster larynx cancer experiments cannot be uniformly repeated. Some other strains of hamsters have not been shown to get cancer at all, and one group of hamsters exposed to smoke did get cancer, albeit not in the larynx, but they lived so much longer than the control hamsters that the researcher could not exclude old age as the cause of the tumors. (Wehner 1976)

Questions have been raised about whether the lesions reported are in fact cancer. In addition, the hamsters used in the experiments that allegedly produced cancers were diseased with viruses. The Sendai virus, which infected the animals in one of the experiments, is known to predispose animals to develop squamous metaplasia of the respiratory epithelia.

7. THE CONTROVERSY REGARDING CONSTITUENTS OF TOBACCO SMOKE

Over the years, some substances found in cigarette smoke or in total particulate matter ("tar") have been implicated as health risks, but later investigation has raised serious

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questions about those implications. For example, the 1967 Public Health Service report noted that selenium, which was reported to be present in some cigarette papers, "has been mentioned as possibly being important in the pathogenesis of human lung cancer." (U.S. PHS 1967) However, researchers have found selenium to be a strong anti-carcinogen. (Zedeck 1984; Schrauzer 1971; Kazantis 1981; Jansson 1977)

The 1967 Public Health Service's report stated that polonium 210 "should be considered as a potential tumor initiator in tobacco smoke." (U.S. PHS 1967) However, the 1981 Public Health Service's report noted that "in the case of polonium 210, a recent indepth study raises doubts on the significance of 210 PO as a factor contributing to lung cancer in smokers." (U.S. PHS 1981) The following year it stated "polonium 210 is present in tobacco and cigarette smoke; however, it is unlikely that these traces represent a major risk for the smoker." (U.S. PHS 1982)

As another example, the 1971 report of the Public Health Service characterized nickel compounds in cigarette smoke as "suspected carcinogens of some importance." (U.S. PHS 1971) Eleven years later, the Public Health Service expressed the following opinion: "it is not likely that nickel plays a

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significant role in the etiology of lung cancer in cigarette smokers." (U.S. PHS 1982)

Although in the early years of the tobacco-health controversy, many critics called for reductions in "tar", nicotine and carbon monoxide levels of cigarettes, more recently some researchers have questioned whether lowered levels of those substances provide any benefits to the smoker. Those questions led the chief of the National Heart, Lung and Blood Institute of the United States National Institutes of Health to assert the following in a 1983 editorial:

> Because tar, nicotine and carbon monoxide are unquestionably the villains, these findings [of no health benefits from consumption of low 'tar', nicotine and carbon monoxide cigarettes] may be viewed as astonishing. Hence, some would probably want to reopen the case against these substances and again question whether it has been scientifically established that smoking is harmful to health.
> (Lenfant 1983)

Condensates of tobacco smoke ("tar") have been found to be carcinogenic when tested by laboratory application to the skin of some animals such as mice and rabbits, as have several polycyclic hydrocarbons isolated from cigarette smoke. However, the 1964 Terry Report to the Surgeon General noted:

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> The results of a number of assays for carcinogenicity of tobacco smoke tars present a puzzling anomaly: the total tar from cigarettes has many times the carcinogenic potency of benzo(a)pyrene present in the tar. The other carcinogens known to be present in tobacco smoke are, with the exception of dibenzo(a,i)pyrene, much less potent than benzo(a)pyrene and they are present in smaller amounts. Apparently, therefore, the whole is greater than the sum of the known parts.
> (1964 Terry Report)

To date, cancer of the lung has not been produced in any of the many experiments where animals totalling in the tens of thousands have breathed whole, fresh cigarette smoke over most of their lifetimes. The most extensive such experiment was conducted by Microbiological Associates, Inc., of Bethesda, Maryland, and funded by the Council for Tobacco Research-USA, Inc. (Chronic Exposure of Mice to Cigarette Smoke 1984) The results of the experiment were related by the Scientific Director of the Council, Dr. Sheldon C. Sommers, in testimony given in March 1982 to the Health and Environment Subcommittee of the United States House of Representatives Committee on Energy and Commerce:

> Almost $14 million went into the project in 12 years. To take account of heredity, inbred mice were used and tested for and vaccinated against respiratory viruses. To

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show these animals could develop the major types of human lung cancers, pure chemical carcinogens were introduced down their tracheas. They were known to metabolize these carcinogens into the biologically active forms. About 20 percent in younger mice and over 95 percent in older mice developed 'human-type' lung cancers as a result of exposures to these pure chemical carcinogens.

Thereafter thousands of mice were exposed daily to fresh whole cigarette smoke of either low nicotine and high tar or high nicotine and high tar content up to maximum tolerance during their whole lives, up to 40 months in some cases. At one point there were 11,000 animal manipulations per day including sham smoking and control mice. After all these years of cigarette smoking practically zero lung cancers developed and not one case of the human type cancer most often blamed on smoking.

There was no question the cigarette smoke had penetrated into their lungs since this was worked out quantitatively. In other experiments mice were primed with intratracheal pure carcinogenic chemicals, then exposed to cigarette smoke during their whole lives. No increase in lung cancer occurred over the incidence found after using

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pure chemicals alone and in one experiment smoking was associated with a reduced lung cancer rate.
(Sommers - H.R. 1982)

8. SUMMARY

There has been a controversy regarding tobacco and health for almost as long as the product has been used by modern man. Because of the concerns that have been voiced, tobacco sales and advertising have been restricted, the product has been heavily taxed, and in some places and certain times, total sales bans have been effected. Yet, notwithstanding their awareness of such attacks, millions of people world-wide have continued to purchase and enjoy tobacco.

In the mid-twentieth century, increasing numbers of reports of studies began to be published which suggested that cigarette smoking might be a factor in lung cancer and other disease causation. Those reports caused a number of governments to investigate the smoking-health question. By the mid-1960s public health agencies in several countries concluded that remedial action was warranted and some concluded that causal relationships existed between smoking and cancer and certain other chronic diseases. Those causal conclusions, however, were not universally accepted by the scientific community. Nor, as exemplified by the experience in the U.S. Congress, were they uniformly or unqualifiedly adopted by the governments involved. Numerous questions regarding the causation theory continued to be

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identified by scientists into the 1980s, including those posed at the 1982-1983 U.S. Congressional hearings. They are still unsolved. They have yet to be answered, particularly those relating to laryngeal cancer causation, and gigantic problems for exploration remain before it can be determined scientifically whether cigarettes cause the chronic diseases at issue in this litigation.

Contrary to the claims of the plaintiff side, the controversy still continues, although less visible as a result of political pressure and the attitudes of the press. As the Vandenbroucke-Greenland discussion demonstrates, it has not quieted away, and in addition, the constitutional hypothesis of Fisher and others, stamped in the beginning to be wrong, seems to gain strength. What if it finally will appear that "wrong" was after all "right" and "right is wrong", what will then happen?

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